

# Cervicogenic headache

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## Cervicogenic **Headache**

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## CHAPTER 1

### Introduction

## INTRODUCTION

Headache has been recognised as a human discomfort since 3000 B.C. Hippocrates, born about 460 B.C. on the Island of Cos in Greece, is considered as 'the father of medicine' in the Western world (1). He recognised the dichotomy of the brain hemispheres and considered the brain responsible for all perception. According to Hippocrates, this dichotomous arrangement could be responsible for the observation that a headache is not confined to one side but sometimes left, sometimes right and sometimes all over the skull (2). Hippocrates saw the brain as an organ of thought and sensation. Causes of illness, such as headache, were either due to internal difficulties or due to outside influences, especially climate, personal hygiene, diet and activity. The four humours corresponding to the four elements were the physiological bases of body function. Harmony of all parts is required for health (1). During the Middle Ages and later the people considered headache to be a phenomenon visited upon them by outside forces as punishment for some type of religious transgression.

Our view of headache disorders have changed since the beginning of this century. However, although everyone knows what a headache is, we know less about the precise pathophysiological disturbances that are perceived as headache than about almost any other comparable symptom. It is a disorder in which symptoms outweigh signs. In this way, headache is unique among the common pain problems since it appears transiently in the majority of people and is still without objective evidence of a pathophysiological substrate.

Headache disorders are extremely prevalent. An epidemiological study demonstrated that the lifetime prevalence of all headache syndromes was 96% and was significantly higher among females (99%) than among males (93%) (3). Among the adult population with headache complaints, 16% are migraine sufferers and 71% have tension-type headache indicating that these two make up the 'bulk' of headache disorders. A study of a sample of the Danish population revealed a one-year prevalence of migraine of 6% in men and 15% in women (3). In the United States, a sample of the population was surveyed in a study that revealed a one-year prevalence of migraine of 6% in men and 18% in women (4). The one-year prevalence of tension-type headache was 63% in men and 86% in women (3). Tension-type headache seems to be more prevalent in women than in men and in both sexes the prevalence tends to decline with age.

Headache syndromes are generally mild or infrequent but when they are severe or frequent, they may cause considerable suffering. It is evident that headache as a medical condition has an enormous impact on all aspects of daily living. It has a negative effect on the quality of life (5) and

increases disability at home and at work and may lead to a significant consumption of drugs (6). The impact of migraine and tension type headache on the quality of life has been demonstrated in previous years (7-10). There are no studies assessing the quality of life for patients with cervicogenic headache (CEH).

Headaches are among the most important causes of sickness absence from work (11). Health care use and a decreased working capacity have been addressed by several epidemiological studies (6, 12, 13). Rasmussen et al. demonstrated that the total loss of workdays per year due to migraine and tension-type headache in the general population was estimated at 270 respectively 820 days per 1000 persons (13). When these figures are extrapolated to the western economy, it is estimated that headache costs society many billions of dollars per year and the productivity losses are profound. Fishman and Black estimate that the mean annual indirect costs per headache patient using the Human Capital method (i.e. the value of what an individual is not doing because he/she is constrained by headache) for 'all headaches' is \$4,304 and \$ 4,796 respectively for men and women (14). The costs caused by absenteeism from work due to patients with cervicogenic headache is not known at this moment because there are no epidemiological studies which involves CEH as a separate headache syndrome. It may be possible that these patients were diagnosed as migraine or tension-type headache. When the cost of lost work days are included, headache disorders become the third most expensive group of neurological disorders after the dementia's and cerebral vascular accidents. The impact of headache due to primary headache disorders on work performance in the general population is substantial and justifies increased alertness to the different headache disorders and adequate therapy.

## CERVICOGENIC HEADACHE

In 1983 Sjaastad et al. introduced the term cervicogenic headache, after a profound study during several years in 22 patients with a rather uniform headache profile, in which he described a distinct headache syndrome which appeared to originate from the neck (15). In the following years many publications from different medical disciplines were published concerning CEH (16-37). Much research has been conducted in the following years by Sjaastad and co-workers into the symptomatic characterisation of patients with CEH, resulting in the first diagnostic criteria of CEH in 1990 (38). This enabled researchers to select patients for trials. Recently refinements of the criteria for CEH have been published by this group (39). Refinements of these criteria included the use of diagnostic nerve blocks as an obligatory point in diagnosing CEH and a bilateral

type of CEH was acknowledged. The use of diagnostic nerve blocks seems to be the obvious method to confirm the diagnosis CEH. However, there are some practical problems leading to false-positive and false-negative outcomes, which limit its usefulness. A point of concern is that during the procedure the physician has to be certain about the proper position of the needle. A diagnostic nerve block should be repeated at the same target point if the physician has any doubt about the procedure. Furthermore it should be stressed that physical examination of the patient during the pharmacological action of the local anaesthetic solution is important in order to correlate the pain response with the maintenance or disappearance of the headache (47).

The term 'cervicogenic headache' remains controversial. Controversy remains regarding the cervical spine's role in this headache syndrome (40, 41). Opponents of the concept say that only in a relatively few patients, lesions in the neck may cause headache. For the majority of patients with headache, however, the neck as a source of the headache is not important. Edmeads states that substantial evidence is lacking in order to decide that CEH exists as an primary headache syndrome separate and distinct from other, more accepted, types of headache (42). He underlined the aspect that CEH could have been mixed up with other accepted headache syndromes, such as migraine without aura and tension-type headache, as a consequence of overemphasising or underemphasising certain headache characteristics in diagnosing headache.

In 1988 the International Headache Society (IHS) introduced new operational diagnostic criteria for headache disorders, cranial neuralgia's and facial pain that provided new opportunities for valid epidemiological and diagnostic headache research (43). Several studies demonstrated that the IHS classification provides satisfactory interobserver reliability for the diagnosis of primary headaches (44, 45). The IHS still does not consider CEH as a separate primary headache syndrome. The current position of the IHS is to employ the category 'headache associated with disorder of the neck' to adapt forms associated with demonstrable neck pathology. Therefore, the IHS considers the concept of CEH, in the absence of evident pathology in the neck, not completely validated. In contrast, the International Association for the Study of Pain (IASP) classification does include CEH (46). The IASP uses general descriptions of the various possible manifestations of CEH, but does not specify whether the presence of clear-cut neck pathology is mandatory to diagnose CEH. The definition of CEH given by Sjaastad and co-workers is very similar to the description given by IASP.

Treatment of most primary headaches is achieved by using drugs. In contrast, the treatment modalities for CEH consists mainly of surgical interventions or manipulative therapy (34, 35). However, the efficacy of those treatments is unclear. Because many of these studies were not con-

trolled and a precise description of the diagnostic criteria was often not included, comparison between the studies is not possible. One must bear in mind that CEH is a clinical diagnosis and is mainly based on the clinician's expertise in taking a careful medical history and performing a complete physical examination of the head and neck. However, the application of diagnostic nerve blocks is essential to confirm the diagnosis CEH.

Of all the headaches, CEH is the least well accepted and the most controversial. Summing up the literature, controversies and questions around CEH contain several aspects: (1) the diagnostic problem is to distinguish CEH from tension-type headache and migraine without aura applying the pertinent criteria (29, 34, 36, 37); (2) the establishment of an efficacious therapy in patients with CEH; (3) an identifiable pathological process (pathophysiological substrate) within the neck capable of eliciting CEH is still lacking; (4) the impact on the quality of life in patients with CEH still remains unknown; (5) epidemiological studies need to reveal the incidence and prevalence of CEH with a uniform definition; (6) the type of diagnostic nerve block(s) to be performed, in which sequence and according which technique, has to be established.

The aim of this thesis is to investigate and to clarify some aspects with regard to the controversies and questions around CEH. Therefore, we sought to answer the following questions:

1. Is it possible to distinguish CEH from migraine without aura and tension-type headache in patients using the diagnostic criteria of each headache syndrome?
2. Can physical examination of the cervical spine in headache patients be done in a reliable way?
3. Are there differences in functional health status among patients with CEH, migraine without aura and tension-type headache?
4. Is cervical zygapophyseal joint neurotomy by radiofrequency lesioning an efficacious treatment modality for patients with CEH?

The outline of this thesis consists of several chapters.

**Chapter two** of this thesis represents a critical review of CEH. In this chapter a survey is given of the history of headaches originating from the neck, which resulted in a concept called CEH defined by Sjaastad and co-workers. A synopsis of certain investigations, such as X-rays and some neurophysiological techniques, is presented. In this chapter the attention is focussed primarily on the pathophysiology, differential diagnosis and treatment modalities for CEH.

**Chapter three** describes the outcome of an 'in vivo' study among patients with migraine or tension-type headache or CEH. The study demonstrates that the reliability to diagnose CEH, when strictly applying the criteria from Sjaastad et al., is similar to the reliability in diag-



nosing migraine and tension-type headache according to the IHS criteria. The same patient group was further analysed in Chapter four.

*Chapter four* presents the results of the assessment of interobserver reliability between two expert headache neurologists in physical examination of the neck in headache patients. The study demonstrates that the reliability scores (Kappa values) were satisfactory in the majority of the physical examination tests of the neck in patients with different primary headache syndromes.

In *Chapter five* the quality of life in patients with CEH is compared with healthy people and those having migraine without aura or episodic tension-type headache.

*Chapter six* reviews the techniques of diagnostic nerve blocks in the cervical area. Suggestions as to their role in the diagnostic work-up of CEH are given. It is recommended to perform the less complex blocks first before moving to the more invasive ones.

*Chapter seven* addresses the first results of a prospective study in patients with CEH, who are treated by radiofrequency lesioning, with a one-year follow-up. It shows that radiofrequency cervical zygapophyseal joint neurotomy leads to a significant reduction in headache severity, in the number of days with headache and in analgesic intake in patients with CEH.

*Chapter eight*, the general discussion, provides a short summary of the results and a critical appraisal of the several studies. Furthermore, the implications of the presented results are discussed and recommendations for future research are given.

*Chapter nine* and *ten*, respectively, consist of summaries in English and Dutch.

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## CHAPTER 2

### Cervicogenic headache: a review

*J.A. van Suijlekom and W.E.J. Weber*

## HISTORICAL PERSPECTIVE

Headache originating from cervical structures is a concept that has received attention since the mid-nineteenth century. The literature on this concept has steadily expanded. Many authors from various medical disciplines have introduced a wide variety of descriptions for headache originating from the neck, including Barré-Lieou syndrome (1, 2), cervical migraine (3), rheumatic headache (4, 5), occipital neuralgia (6, 7), céphalée cervicale (8, 9), post traumatic cervical headache, occipital myalgia-neuralgia syndrome (10), spondylogenic headache (11), cervical headache (12) or cervicogenic headache (CEH) (13).

Schützenberger, a Strasbourg physician, probable was the first physician to recognise that headaches could arise from the cervical spine. Bärtschi-Rochaix recalled that in 1853 Schützenberger described a headache that might be caused by some pathology from the cervical vertebrae (3). In 1913, Gordon Holmes described a headache stemming from the neck that was associated with tender nodules in the posterior neck muscles, which were ascribed to fibrositis (4). This gave rise to the notion of 'rheumatic' headache, an idea shared by some contemporaries (5, 14).

In 1926 Barré published a report in which he linked this headache to sympathetic nerves surrounding the vertebral artery in the cervical area and termed it 'syndrome sympathique cervicale postérieur' (15). Barré hypothesised that the cause of this syndrome was spondylarthrosis of the cervical spine irritating the vertebral nerve – the sympathetic nerves accompanying the vertebral artery - which surrounds the vertebral artery. Others adopted this hypothesis and proposed other lesions in the cervical spine that could cause headache (16-18). Lieou, another French physician, published a thesis in 1928 about this topic named: 'syndrome sympathique cervical postérieur et arthrite chronique de la colonne vertébrale cervicale', in which he emphasised the role of the cervical spine in eliciting headache (2). The symptoms described by the author were headache with occipital preference, vertigo, acoustic symptoms, visual disturbances and difficulties on swallowing. A number of articles on this so-called Barré-Lieou syndrome were published in the French literature in the thirties (1, 19, 20). Bärtschi-Rochaix published a monograph on this topic in 1949 and renamed it 'migraine cervicale' (21). He argued against irritation of the vertebral nerve as the pathogenic mechanism of this headache. After various experimental studies he considered blood flow alterations in the vertebral artery, due to displacement by osteophytes, as the chief factor in the pathogenesis, rather than maladjustment of the sympathetic nerves around the vertebral artery. Afterwards, studies in humans and in monkeys revealed that the so-called vertebral nerve between each segment from C3 to C7 consists of a series of intersegmental neural arcades formed by communications between grey rami communicantes from the

sympathetic trunk and ventral rami of C3 to C7 (22). Above the level of C3 the grey rami communicantes are not involved in these connections and the vertebral artery is accompanied by direct branches from the C1 – C3 ventral rami. This implicates that, instead of a single 'vertebral nerve', there is a separate nervous innervation of the different parts of the vertebral artery. Therefore, irritation of grey rami by mid and lower cervical lesions would hardly influence distal branches of the vertebrobasilar vasculature. This was confirmed by experiments in which direct electrical stimulation, using platinum hook electrodes, of either the vertebral nerve, or the cervical sympathetic trunk, failed to influence vertebral blood flow significantly while sympathetic stimulation reduced the carotid blood flow with 70% due to corresponding vascular resistance increase (22). Thus, neither anatomic nor physiologic evidence was found supporting the 'vertebral nerve irritation hypothesis' (3, 23).

According to Bärtschi-Rochaix, cervical migraine is a functional and reversible ischaemic syndrome of the vertebral artery (3, 21, 24). In his 1968 publication he stated that cervical migraine is the consequence of degenerative changes in the cervical vertebrae and arteries, with trauma as a potential anticipatory event. Compression of the vertebral artery would occur either in the region of the uncovertebral joints or adjacent to the odontoid process. In a comprehensive description Bärtschi-Rochaix wrote upon the multilateral aspects of this headache in a group of 33 patients (21). Nearly all patients had a unilateral headache radiating to the temporo-parietal and frontal regions with subjective or objective signs of neck involvement, such as a reduced mobility of the cervical spine, on the same side as the headache. Attack-related phenomena, such as ipsilateral radiating symptoms in the upper extremities, paresthesias, dizziness and blurred vision, accompanied the headache attack in patients. The most typical radiological findings, i.e. deformity of the uncovertebral joints, were localised at the C3-C4 and C5-C6 levels. Bärtschi-Rochaix assumed that the uncovertebral deformities caused an intermittent reduction of the blood flow in the vertebral artery. In resemblance with classical migraine, which was considered to be caused by a reduction of carotid blood flow in those days, he termed this headache 'migraine cervicale'.

In 1939, Hadden described an unilateral 'boring' pain in the suboccipital region spreading to the ipsilateral temporal area and even to the retro-orbital region (7). Some patients complained of photophobia. Pressure over the greater and / or minor occipital nerve produced intense pain during the attack. Hyperesthesia in the sensory area of the greater occipital nerve was observed. He referred to this syndrome as 'occipital neuralgia'. Hadden divided the occipital neuralgia's into three groups: acute-, intermittent- and chronic occipital neuralgia. He stated that the term



'occipital neuralgia' embraced all pain experienced in the posterior part of the head. He asserted that the occipital nerves might become involved in 'chronic inflammatory lesions' at the point where they penetrate the tendinous portion of the trapezius muscle. As treatment he advocated injection with a local anaesthetic solution at the greater occipital nerve. Nowadays occipital neuralgia is defined in the International Headache Society (IHS) classification as a paroxysmal, stabbing pain accompanied by hypoesthesia or dysesthesia in the distribution of the greater or minor occipital nerves. The continuous occipital pain as described by Hadden and Sigwald is not acknowledged in the IHS criteria (6, 7, 27). The IHS diagnosis requires tenderness to palpation in the sensory area of the greater or minor occipital nerve (27). Mandatory in the IHS criteria is that temporary relief is achieved after anaesthetic block of the nerve. According to Hadden's description, some patients with chronic occipital neuralgia's type would probably fulfil the present criteria for CEH.

In 1938 Cyriax induced headache in volunteers by injecting hypertonic saline into the occipitalis muscle, the suboccipital region, and into the posterior upper cervical muscles (25). The more rostral stimuli evoked pain in the forehead, while the more caudal stimuli evoked pain in the occiput. Campbell and Parsons stimulated systematically the occipital condyles and the midline tissues from the suboccipital region to the C4-C5 level, and mapped the incidence of referred pain in predetermined regions of the face, head, neck and shoulder (26). The rostral stimuli produced referred pain to the facial and orbital regions. The more caudal stimuli showed referred pain into the occiput, suboccipital regions, posterior neck and shoulder. These studies established that headache could be produced by noxious stimulation of muscles in the cervical spine.

During the years 1940-1950 some investigators proclaimed theories to understand why cervical pathology could lead to headache (28-30). They postulated a neural connection between the upper cervical nerves and the fifth cranial nerve.

Hunter and Mayfield hypothesised in 1949 that recurrent attacks of severe hemicranial pain could be caused by compression of the C2 nerve root or greater occipital nerve between the posterior arches of the atlas and axis (31). They based their hypothesis on observations in cadavers, in which they demonstrated that movements of the atlanto-axial joints during manipulation could traumatise the second cervical nerve. In their clinical study the majority (8/11) of their patients had suffered a neck injury. Three patients without a neck injury had similar headache complaints. Patients complained of sudden attacks of pain in the suboccipital region, always on one side of the head, radiating to the vertex, temporal area and usually to the area around the eye. The duration of the attacks varied from several minutes to several days, the majority lasting from 2 to 3 hours. Anaesthetic block of the C2 nerve root with procaine abolished the

head pain. Anaesthetic block of the greater occipital nerve interrupted the head pain too, but to a lesser extent. They treated their patients either with neurectomy of the greater occipital nerve or intraspinal section of the sensory nerve root of C2 or section of the sensory roots of C2 and C3. In the trauma group there was a striking relief of symptoms after the surgical procedure. In the non-trauma group with almost identical complaints there was no relief of symptoms. Although follow-up in this study was too short to be conclusive, it led to an increasing popularity of greater occipital nerve blocks, C2 nerve blocks and posterior rhizotomies. In 1955, Mayfield was less enthusiastic about the earlier success of their treatment (32). More recently, Bogduk has shown that the C2 nerve root and the greater occipital nerve cannot be adequately lesioned in the way proposed by Hunter and Mayfield (33).

The possible role of cervical discs as a headache generating factor was pointed out by several authors (34-36). Raney and Raney stated that these headaches are often unilateral but may also be bilateral and may be elicited by certain head movements. The duration can be short or lasting longer than seventy-two hours and may be associated with nausea and vomiting. In 1959, Cloward described the results of a study of provoked cervical discography (37). He demonstrated that the patterns of referred pain were constant whether the stimulus was produced by needle puncture on the external surface of the disc or by injection of the disc itself with contrast medium. The pain was assumed to be due to irritation of peripheral nerve fibres in the disc by direct stimulation or by the increase in intradiscal pressure which is transmitted to the nerve fibres in the periphery of the disc. Cloward emphasised the potential role of the cervical sinu-vertebral nerves in referred pain syndromes of shoulder and upper arm, caused by the cervical intervertebral discs (38). After provocation, each disc level would produce a typical radiation pattern to the region of the shoulder, muscles along the vertebral border of the scapula and the upper extremity. However, posteriorly provoked disc pain differed from anteriorly provoked disc pain; it is not confined to the vertebral border of the scapula but spreads out in a fan-shaped band over the scapula and into the upper arm. It is important to note that Cloward's patients did not report headaches or pains radiating to the (sub)occipital region and the face. In contrast, Raney et al. and Mayfield have indicated that intervertebral disc lesions in the cervical spine, such as narrowing of the disc with or without proliferation of bone, are frequently associated with headaches radiating to the occipital region, the frontal region and are often associated with nausea (34, 39, 40). Other authors considered arthrosis of the upper cervical synovial joints as a source of headache in cervical spondylosis (41, 42). Lord Brain considered spondylosis as a common and important cause of headache beginning in middle life and later (41).

In 1983 Sjaastad et al. introduced CEH as a clinically defined syndrome (13). In the following years the clinical picture of CEH was described in more detail which resulted in the first criteria for CEH in 1990 (43). A pathophysiological model for CEH was described by Frederick Kerr and termed 'the Kerr principle' by Bovim (44). Kerr published several papers in which he hypothesised a pathogenetic model for headache stemming from the cervical region and the posterior fossa (45-48). Central in the mechanisms of CEH is the trigeminocervical nucleus, as a relay station for referred headache stemming from a nociceptive source in the cervical spine. The neuro-anatomy of the trigeminocervical nucleus implies that the upper three cervical levels are the most likely involved. As a consequence, any of the structures innervated by the first three cervical segmental nerves would be a potential source of referred pain to the head. However, the middle and lower part of the neck may contribute to head pain as well (49-51).

The concept of CEH as proposed by Sjaastad et al. is still controversial (52, 53). Edmeads agrees that congenital and acquired anomalies of the craniovertebral junction, ankylosing spondylitis or severe rheumatoid arthritis, may produce headache. In absence of such pathology in the cervical spine, its relation with headache remains unproven. He concludes that CEH requires more substantial evidence before it can be accepted as a primary headache syndrome. Lance described the clinical picture of CEH in his classical textbook, but concludes that it is possible that CEH is a variant of migraine triggered from the upper cervical spine in a manner comparable with other forms of afferent stimulation such as light and noise (23).

Bogduk considers the clinical definition of CEH according the criteria from Sjaastad and coworkers as not reliable. According to him none of these clinical criteria, nor any combination of them, is unique to CEH, as the same features can occur in migraine and tension-type headache. In Bogduk's view, the gold standard to diagnose CEH is a positive double-blinded, placebo controlled diagnostic block with a local anaesthetic solution directed to a nervous structure or to an anatomical structure such as the intervertebral disc in the neck (12).

## NOMENCLATURE AND CLASSIFICATION

CEH is by definition a headache originating from the neck. This terminology presents some difficulty. Another proposed term, 'cervical headache' is problematic since a headache can never be cervical. The more appropriate term is 'cervicogenic headache', which implies an ache felt in the head, but originating in the neck. The term 'cervicogenic' reflects the origin of the pain, without specifying which anatomic structures may be the source of the pain.

The term CEH was introduced by Sjaastad and colleagues in 1983 after a thorough clinical study during several years in a group of 22 patients with a rather uniform headache syndrome (13, 54). The authors extensively described the clinical manifestations of the headache complaints in this patient group. During the following years more studies on CEH were published giving rise to a more comprehensive picture of CEH (55-66). In 1990, in an effort to standardise research in CEH, Sjaastad et al. published criteria to establish the diagnosis (43), with a recent revision in 1998 (Table 1A.)(67).

However, despite its long history and many clinical studies, the concept of CEH is still controversial (23, 53, 68). The IHS classification does not include CEH as a primary headache syndrome (27). The IHS classification does include 'headache associated with disorder of the neck', in order to accommodate headaches in close relation to a disorder of the neck. The IHS criteria are: A) pain localised to neck and occipital region which may radiate to forehead, orbital region, temples, vertex or ear; B) pain is precipitated or aggravated by special neck movements or sustained neck posture; C) at least one of the following: 1) resistance to or limitation of passive neck movements; 2) changes in neck muscle contour, texture, tone or response to active and passive stretching and contraction; 3) abnormal tenderness of neck muscles; D) radiological examination reveals at least one of the following: 1) movement abnormalities in flexion/extension; 2) abnormal posture; 3) fractures, congenital abnormalities, bone tumours, rheumatoid arthritis or other distinct pathology (not spondylosis or osteochondrosis). A headache of cervicogenic origin without radiological evidence of pathology of the cervical spine and/or persisting for more than one month, after treatment or spontaneous remission of the underlying disorder, cannot be defined according to the IHS (27).

In contrast, the International Association for the Study of Pain (IASP) classification does include CEH as a primary headache syndrome (69). Descriptions of the various clinical manifestations of CEH in the IASP classification are in accordance with the criteria of Sjaastad et al. (67). However, stringent application of the criteria as settled by Sjaastad et al., see Table 1A., is not required.

## CLINICAL PICTURE

CEH is, in principle, a side-locked unilateral headache, but it may also be bilateral ('unilaterality on two sides'). The pain typically starts in the neck or at the occipital-nuchal area and spreads to the ipsilateral oculo-fronto-temporal region where the maximal pain is frequently located. A diffuse, ipsilateral shoulder and arm pain of a rather vague, non-radicular nature, or occasionally of a radicular nature may co-exist. The intensity of

**Table 1A.Criteria for cervicogenic headache.**

**MAJOR CRITERIA**

- I. Symptoms and signs of neck involvement:
  - a) Provocation of an irradiating head pain, similar to the spontaneously occurring one:
    - 1) By neck movement and/or sustained, awkward head positioning, and/or
    - 2) By external pressure over the upper cervical or occipital region on the symptomatic side.
  - b) Restriction of the range of motion (ROM) in the neck
  - c) Ipsilateral neck, shoulder, or arm pain of a rather vague, nonradicular nature, or – occasionally – arm pain of a radicular nature
- II. Confirmatory evidence by diagnostic anaesthetic blocks.
- III. Unilaterality of the head pain, without side shift.

**PAIN CHARACTERISTICS**

- IV. Non-throbbing pain, usually starting in the neck
  - Episodes of varying duration, or
  - Fluctuating, continuous pain

**OTHER CHARACTERISTICS**

- IV. Only marginal effect or lack of indomethacin.
  - Only marginal effect or lack of effect of ergotamine and sumatriptan.
  - A certain female preponderance.
  - Head or indirect neck trauma by history, usually of more than only medium severity

**OTHER DESCRIPTIONS OF LESSER IMPORTANCE**

- V. Various attack-related phenomena, only rarely present, and/or moderately expressed when present.
  - a) Nausea
  - b) Phonophobia and photophobia
  - c) Dizziness
  - d) Ipsilateral 'blurred vision'
  - e) Difficulties on swallowing
  - f) Ipsilateral edema, mostly in the periocular area

**Cervicogenic headache:**  
summary of minimum requirements for diagnosis

	Confirmatory combination	Provisional combination <sup>(1)</sup>
I. Neck involvement	Presence of	
a) Precipitation of attacks	a1 and/or a2	
1) Subjectively		
2) Iatrogenically		
b) Reduced range of motion in neck		Present
c) Ipsilateral shoulder/arm pain		Present
II. Anaesthetic block effect	Positive	Positive
III. Unilaterality without sideshift	Present <sup>(2)</sup>	Present <sup>(2)</sup>

<sup>(1)</sup> The provisional combination is tentative

<sup>(2)</sup> In nonscientific work 'unilaterality without sideshift' does not need to be present.

the headache is experienced mostly as moderate with a non-throbbing character. It is a continuous, dull, boring, dragging pain, which can fluctuate in intensity. Attacks may be provoked by particular neck movements or by external pressure applied to ipsilateral tender points in the neck or occipital area. The duration of the solitary headache attack or exacerbation may range from a few hours to several days. Sometimes it lasts several weeks. Sooner or later the solitary attacks may be substituted by a pattern of a chronic fluctuating headache. Symptoms which link this headache to the neck are essential such as a reduced range of motion in the neck, precipitation of the attack by mechanical stimuli or neck movements. Associated symptoms like nausea, photo- and phonophobia, dizziness, ipsilateral 'blurred' vision and dysphagia may be present but are generally not pronounced. Females are more frequently affected than males. Although trauma to the head and/or neck may precede the onset of the syndrome, many patients do not report a history of any neck or head injury.

An essential diagnostic feature of CEH is a positive response, i.e. a transient pain-free period, after an appropriate diagnostic nerve block. These diagnostic blocks should be directed to the nerve(s) or anatomical structure(s) suspected of mediating or causing CEH. Appropriate blocks in the neck or head should include structures capable of causing CEH such as: the greater occipital nerve, minor occipital nerve, zygapophyseal joints (facet joints), segmental nerves and eventually intervertebral discs (50, 67, 70).

Radiological investigative methods such as standard X-ray of the cervical spine and functional radiographs in flexion and extension, cerebral and cervical computer tomography, cerebral angiography and cervical myelography, do not contribute to a diagnostic work-up of CEH (57, 58).

## EPIDEMIOLOGY

Early estimates of the prevalence of CEH varied considerably, with some authors considering it as a relative rarity (13) while others regard the cervical spine as the major source of headaches seen in general practice (71). Since the introduction of the classification system and diagnostic criteria for the different headache syndromes more reliable epidemiological studies have been done (27, 43, 67).

Nilsson performed a questionnaire study to estimate the prevalence of CEH using the IHS criteria (72). In this study, 826 adults were randomly chosen from the population register in a Danish city. The prevalence of CEH in the general population in Nilsson's study was 2.5%. He showed that the prevalence of CEH in a subgroup of patients experiencing frequent headaches (5 or more days in the previous month) was 17.8%. However, it is difficult to estimate the true prevalence rate of CEH based on the current IHS criteria (50). Pfaffenrath and Kaube, using the criteria

from Sjaastad and co-workers, found in a hospital-based study a prevalence rate of 13,8% among 5520 headache sufferers' (61). In another hospital-based study of D'Amico et al. the prevalence of CEH according the criteria from Sjaastad et al. was 0.7% among 440 headache patients. Monteiro, using the criteria from Sjaastad et al., showed in a population study a prevalence for CEH of 1% in headache patients when 6 of a total of 6 criteria were employed (73). The prevalence rate increased to 4.6% when only 5 of these criteria were used.

It is difficult to assess the true prevalence rate of CEH from these aforementioned studies because: 1) different criteria for CEH have been used in the studies; 2) varying epidemiological study designs were employed i.e. population-based studies versus clinic-based studies. General practioners are the physicians most frequently consulted for headache problems and not the neurologist (74). As a consequence, hospital-based studies suffer from substantial selection bias. It is known that most migraine studies are clinic-based, yet less than 15% of migraine sufferers ever consult a neurologist, and fewer than 2% consult headache specialists (74-76). It is clear that an extensive epidemiological population-based study is needed to assess the true prevalence of CEH according the criteria from Sjaastad et al.

A female preponderance for CEH, diagnosed according the criteria from Sjaastad et al., has been confirmed by different authors (44, 54, 58, 61, 77).

## PATHOPHYSIOLOGY

The primary afferent nociceptor is generally the initial structure involved in nociceptive processes. The cervical spine and its related body structures contain nerve endings (nociceptors) which are responsive to (noxious) mechanical, thermal and chemical stimuli. Depending on the response characteristics of the nociceptor, stimulation results in propagation of impulses along the afferent fibres toward the spinal cord. The receptors associated with transmission of noxious information can be divided in two main categories: A $\delta$  mechanothermal fibres and C polymodal fibres (78). These fibres belong to the small fibres system, in contrast to the large fibre system (A $\alpha$  and A $\beta$ ) which transmits stimuli generated by touch and pressure. Most forms of pain arise from direct activation or sensitisation of primary afferent neurons, especially the C fibre polymodal nociceptors (78). Injury of structures in the neck such as strain injuries to muscles or ligaments, pathological changes at the zygapophyseal joints or discs etc., may stimulate the C fibre nociceptors. Large and small diameter primary afferents have their cell bodies in the dorsal root ganglia. Pain impulses from the occipital region of the head and the neck enter the spinal cord via de C1-C7 roots. The spinal terminals of the small fibres enter the cord



in the lateral portion of the entry zone and have collateral branches, which may ascend or descend for up to three segments, in Lissauer's tract, before synapsing in the dorsal horn laminae (48, 79).

The role of the trigeminal nucleus in relation to pain in face and neck was established by several authors many years ago (28-30, 80). The trigeminal nucleus is divided in the main sensory nucleus and the spinal tract nucleus, which is located far caudally in the cervical spinal cord. The spinal tract nucleus comprise a rostral subnucleus oralis, a middle subnucleus interpolaris and a caudal subnucleus caudalis. The nucleus caudalis is the most caudal subdivision of the spinal tract nucleus (80). The grey matter of the brain-stem that constitutes the pars caudalis of the spinal tract nucleus of the trigeminal nerve, is continuous with the grey matter of the dorsal horns of the spinal cord (81). There is no intrinsic anatomical feature that demarcates where the spinal nucleus caudalis ends and the grey matter of the spinal cord begins. This functional continuum column of neural cells formed by the pars caudalis of the spinal tract nucleus of the trigeminal nerve and the grey matter of the upper three cervical spinal cord segments could be regarded as the trigeminocervical nucleus (81).

Marked convergence of primary afferents of the upper three or four cervical roots with those of the trigeminocervical nucleus has been established (47, 48). Kerr used the term 'convergence' to indicate that fibres from different sources converge on the trigeminocervical nucleus, but that implied nothing about actual anatomical or physiological convergence on individual neurons. In an animal experiment, investigating the structural relationship between trigeminal and cervical afferents, Kerr concluded that the contribution of the C1 root was negligible (45). However, later animal studies showed a substantial larger contribution from the C1 root to the trigeminocervical nucleus (48, 82, 83). Connections between the trigeminocervical nucleus and the upper four cervical roots are the neuro-anatomical substrate for the spreading of pain from the cervical area to the head (45-47, 84, 85). Other physiologic studies have supported the anatomic evidence for widespread termination of trigeminal afferents within the nucleus caudalis (86-88). This phenomenon of convergence of afferent input at the nucleus caudalis from the head and cervical region and from the main sensory trigeminal nucleus may serve as a pathway of referred pain impulses from the neck to the frontal-temporal region of the head and vice versa (85). This convergence forms the neuro-anatomical basis for the concept of CEH. This concept also provides an anatomical explanation for referral of pain to the occipital region and upper neck in migraine (85).

The nucleus caudalis contains two classes of neurons associated with sensory processing that are remarkably similar to those reported in the spinal cord (87). The first class is termed 'nociceptive specific'; the second class is termed 'wide dynamic range' neurons. Some 'wide dynamic range'

neurons receive only A $\beta$  and A $\delta$  input, whereas others receive strong (polysynaptic) C-fibre input, and their responses to C-fibre activation typically 'wind up', meaning they increase with repetitive stimulation (89). Neurons in the nucleus caudalis also project within the trigeminal tract to the more rostral sensory nuclei (90, 91). Studies have shown that neurons of the nucleus caudalis may hyperpolarise primary afferent terminals synapsing on neurons in the more rostral sensory trigeminal nuclei (92-95). Brief activation of unmyelinated primary afferents may trigger a prolonged central hyperexcitability, which also converts 'nociceptive specific' cells into 'wide dynamic range' cells and enlarges their receptive fields. Normally 'wide dynamic range' cells do not signal pain in response to non-noxious tactile stimulus. However, if they become sensitised and hyperexcitable a non-noxious tactile stimulus will be perceived as painful. Such mechanisms may cause normal input, from muscles, ligaments, zygapophyseal joints etc., to become painful (96). The concept in CEH is that nociception originates from anatomical structures in the occipital region of the head and the neck. Whether sensitisation of 'wide dynamic range' neurons play a role in the pathogenesis of CEH needs to be established.

The C2 spinal cord segment is an important relay for afferent pain fibres. It connects to the dorsolateral tract, the pathway for multisegmental pain impulses from muscles, ligaments, joints, discs and spinal nerves. It also relates to the descending trigeminal spinal tract through which run most of the intra-cranial pain sensory fibres (58). In CEH the C2 root probably plays a central role in the transmission of pain impulses (63, 70). Animal studies have demonstrated that stimulation of the greater occipital nerve increases the metabolic activity in the nucleus caudalis and in the cervical dorsal horn at the level of C1 and C2 (97). This metabolic activity seen with greater occipital nerve stimulation in cats is likely to reflect increased neuronal activity in both the cervical and trigeminal system. In another experiment, Goadsby et al. demonstrated an increase of calcitonin-gene-related peptide (CGRP) in the venous jugular blood during stimulation of the trigeminal ganglion in humans as well as cats (98). CGRP is considered as a marker of trigeminal activation. However, Vincent et al. showed that stimulation of the greater occipital nerve in rats decreased CGRP levels (99). Vincent et al. hypothesised that stimulation of the greater occipital nerve in the rat inhibited the trigeminal system. These results are in contradiction with the findings of Goadsby et al., who demonstrated a metabolic activation, using the 2-deoxyglucose autoradiography and quantitative densitometry technique, of the nucleus caudalis of the trigeminal tract (97). Although the 2-deoxyglucose method cannot determine if increased activity is an excitatory or inhibitory phenomenon, but given that these are second order neurons, an inhibitory phenomenon must be unlikely. A possible explanation for the contradictory results of Goadsby and Vincent may be due to an inter-species variability or

methodological differences such as a time span between blood sampling and stimulation. However, important to remark is the fact that, in the study from Vincent et al., the values of CGRP were different from the stimulated side compared to the non-stimulated side. This suggests that cervical input may influence CGRP levels (99). The data from Goadsby et al. suggest that the link between neck pain and headache may be a referral of poorly localised afferent input on second order neurons of the nucleus caudalis and the C1-C2 dorsal horn cells (97). This group of cells is usually referred as the trigeminocervical nucleus (81).

Animal studies suggest that the (retrograde)activation of the trigeminovascular system is the final common pathway for migraine (100). The trigeminovascular system is also the major pain signalling system of the brain and the final common pathway for headache disorders as meningitis and arteriovenous malformation (101). Blood levels of CGRP rise in patients with common as well as classical migraine (102) and after stimulation of the superior sagittal sinus in the cat (103). Stimulation of the superior sagittal sinus revealed involvement of the nucleus caudalis to the level of the dorsal horn of C2 (104). In CEH, the exact role of the trigeminovascular system in the pathophysiology of CEH is still unclear.

Olesen proposed a concept in which he stated that headache may be due to an excess of nociceptive input (105). In his vascular-supraspinal-myogenic concept, the neurons of the trigeminal nucleus caudalis play a central role. According to this model, perceived headache intensity is the sum of nociception from cranial and extra cranial tissues converging upon the nucleus caudalis neurons. He used this model to explain the clinical and pathophysiological observations in migraine and tension-type headache. It is not unlikely that an excess of nociceptive input from the cervical spine may sensitise these neurons too and which may lead to headache (106). It has been demonstrated that repetitive C-fibre afferent input facilitate 'wide dynamic neurons' at the dorsal horn. This phenomenon, known as 'wind-up', is characterised by a time-dependent increase in spinal cord responsiveness to subsequent afferent input (107).

Transient relief or long-lasting reduction of pain has been demonstrated in CEH patients by anaesthetic blockade of the C2 root or the greater occipital nerve (medial branch of the dorsal ramus C2) (13, 58, 108-110). However, this does not imply that CEH emanates from the C2 root itself or from sources innervated by the C2 segmental nerve. Goadsby et al. and other authors suggest that the therapeutic effect of nerve blocks and surgical approaches to cranial pain syndromes may be explained more by the general reduction of afferent nociceptive traffic in the analogous human neuronal elements, than in the peripheral structures that are manipulated (97, 110-112). It is still unclear why some patients with cervical pain develop headache, i.e. CEH, while in other patients the neck pain is not accompanied with headache. However, application of

Olesen's concept with the proposition of a (genetic) prone supraspinal facilitation in patients with CEH, could be a possible explanation for this.

## MEDICAL HISTORY

A complete and accurate medical history is an important aspect of any initial consultation, and in particular those for headache. In the majority of patients a systematic medical history will establish the diagnosis, or lead to a differential diagnosis, which, in case of CEH, may be further confirmed by physical examination of the cervical spine and a diagnostic nerve block. The use of a semi-structured questionnaire to diagnose headache patients is recommended in research. Such a semi-structured questionnaire should contain questions that correspond with the different criteria of the headache syndromes. In 1988, the IHS published the first international headache classification including operational diagnostic criteria for nearly all headache syndromes (27). The diagnostic criteria for CEH were published in 1990 with a recent revision in 1998 (Table 1A) (43, 67). The diagnostic criteria for migraine and tension-type headache are summarised in Table 1B and Table 1C, respectively.

The diagnostic problem in CEH is to distinguish it from migraine without aura and tension-type headache (70, 109, 113). However, recently Vincent and Luna demonstrated in a prospective study using data from patient records, that CEH clearly differs from migraine without aura and tension-type headache and that the existing criteria to distinguish these headache syndromes were adequate (114). The most significant differentiating aspects were the site and radiation of the pain, temporal pattern and induction of attacks from neck posture, movements, and/or by external pressure at structures in the neck and occipital region.

## PHYSICAL EXAMINATION

A general physical and neurological examination should be performed following the medical history in each headache patient in order to exclude organic disorders as the cause of the headache. The emphasis of the physical examination will naturally be on the head, neck and nervous system, but other organ systems should not be neglected. Here we will restrict ourselves to the physical examination items in regard to CEH. Physical examination of the neck and the head plays a crucial part in diagnosing CEH, according to the criteria from Sjaastad et al., in order to distinguish it from migraine without aura and tension-type headache (67). The IHS criteria contain no items for physical examination to diagnose migraine and tension-type headache because they are not relevant to diagnose these headache syndromes (27).

Relevant issues of the physical examination of the neck and the head

**Table 1B.Criteria for migraine without aura**

- A. There have been at least five attacks fulfilling criteria B, C and D listed below.
- B. The headache attacks last between 4 and 72 hours (untreated or unsuccessfully treated).  
Note: In children below age 15, attacks may last between 2 and 48 hours. If the patient falls asleep and wakes up without migraine, the duration of the attack is until time of awakening.
- C. At least two of the following pain characteristics are present:
  - 1. Unilateral location.
  - 2. Pulsating quality.
  - 3. Moderate or severe intensity, inhibiting or proinhibiting daily activities.
  - 4. Aggravation by walking stairs or similar routine physical activity.
- D. At least one of the following symptom groups is present during the attack:
  - 1. Either nausea or vomiting.
  - 2. Both photophobia and phonophobia.
- E. At least one of the following applies:
  - 1. History, physical and neurological examinations do not suggest one of the following disorders:
    - 1) chronic post-traumatic headache;
    - 2) drug-induced headache;
    - 3) other specified headache syndromes or cranial neuralgias.
  - 2. History, physical, or neurological examinations do suggest such a disorder, but it is ruled out by appropriate investigations.
  - 3. Such a disorder is present, but the migraine attacks do not occur for the first time in close temporal connection with the disorder.

## Table 1C.Criteria for tension-type headache

- A. There have been at least 10 previous headache episodes fulfilling criteria B-D listed below.
- B. The headache lasts from 30 minutes to 7 days
- C. At least two of the following pain characteristics are present:
  - 1. Pressing or tightening (non-pulsating) quality.
  - 2. Mild or moderate intensity (the pain may inhibit, but does not prohibit activities).
  - 3. Bilateral location.
  - 4. No aggravation by walking stairs or similar routine physical activity.
- D. Both of the following apply:
  - 1. There is no nausea or vomiting (anorexia may occur).
  - 2. There is no photophobia and phonophobia occurring together (but one or the other may be present).
- E. At least one of the following applies:
  - 1. History, physical and neurological examinations do not suggest one of the following disorders:
    - 1) chronic post-traumatic headache;
    - 2) drug-induced headache;
    - 3) other specified headache syndromes or cranial neuralgias.
  - 2. History, physical, or neurological examinations do suggest such a disorder, but it is ruled out by appropriate investigations.
  - 3. Such a disorder is present, but the tension-type headache attacks do not occur for the first time in close temporal connection with the disorder.

are: 1) the presence of symptoms and signs in the occipital region and the neck in patients with CEH in regard to the criteria from Sjaastad et al.; 2) can a physician reliably assess these signs and symptoms in these headache patients? In a study among 500 primary headaches Leone et al. demonstrated that unilateral headache triggered by head movement or sustained awkward head positioning was present in 2 patients (0.4%) (113). Pfaffenrath et al. showed that in the majority of patients, diagnosed as CEH, precipitation or enhancement of the headache could be provoked by neck motion (58). Vincent and Luna demonstrated in their study, which included 33 CEH patients, 65 migraine patients and 29 patients with tension-type headache, that headache triggered by neck motion was present in 27 (81%) of the patients diagnosed as CEH, while this criterion was present in 3 (10.3%) respectively 0 (0%) patients diagnosed as tension-type headache or migraine (115). The study from Pfaffenrath et al. demonstrated the presence of trigger points in most patients (58). In contrast, in the study from Leone et al. not one headache was triggered by external pressure (113). Vincent and Luna showed that headache elicited by external pressure was present in 25 (75%) CEH patients. This criterion was also present in 2 (6.9%) patients diagnosed as tension-type headache but in none of the migraine patients. An explanation for the low frequency of symptoms and signs of neck involvement in the study of Leone et al. could probably be attributed to the biased population of headache patients. Patients in the study of Leone et al. were diagnosed as migraine or tension-type headache and he analysed them retrospectively whether the criteria for symptoms and signs of neck involvement were present yes or not. The conclusion of these findings is that the presence of symptoms and signs of involvement of the neck and occipital region are shown in the majority of patients with CEH but not, or at least to a much lesser extent, in patients with migraine or tension-type headache.

The second point is the reliability of the physical examination of the neck and the occipital region in headache patients. Normal volunteers and patients with non-specific chronic neck pain have been subjected to reliability studies of diagnostic tests in physical examination of the neck (116-121). None of these reliability studies have been conducted in patients with headache and these studies were mainly performed by other medical disciplines such as physiotherapists and chiropractors. The kappa values varied between 0.00 and 0.80, indicating a poor to good reliability.

## MANUAL DIAGNOSTIC EXAMINATION

Manual examination is a clinical method of physical examination used by physicians for musculoskeletal medicine and physiotherapists to determine the presence or absence of symptomatic spinal segmental joint dysfunction. Cervical segmental joint dysfunction is regarded as a suffi-

cient stimulus for CEH (122-124). However, cervical segmental dysfunction can be present in other headache syndromes as well, such as tension-type headache and migraine (125, 126). Performing a manual examination, several components of segmental spine dysfunction can be identified such as 1) hypomobility; 2) hypermobility; 3) tenderpoints in muscles; 4) hypertonic muscles; 5) restricted and/or painful movements of the neck (125).

Jaeger reported in a descriptive study of 11 CEH patients that myofascial tender (trigger) points may be an important pain producing mechanism (127). Segmental cervical joint dysfunction was found in the majority of these patients. Unfortunately there was no control group in that study to compare. Vernon et al. found high frequencies of tender points in the upper cervical region together with a greatly reduced or absent 'cervical curve' in patients with tension-type headache as well as with migraine (125). A prospective controlled study demonstrated that cervical segmental dysfunction in the neck, between migraine and tension-type headache patients versus controls, was not statistically significant for a single performed test (126). Only when two or more combined abnormal tests were present, a 0.05 confidence level of significance was reached. Maigne, a French orthopaedic surgeon, has put forward the concept of painful intervertebral dysfunction in the upper cervical spine as a trigger for headache. He suggested that for headache of cervical origin due to painful intervertebral dysfunction, the most frequent dysfunctional segment is located at the C2-C3 level that projects to the relevant dermatome (128). The pain in the dysfunctional segment is thought to originate from the zygapophyseal joints. The ability of a manipulative therapist to diagnose symptomatic cervical zygapophyseal joint syndromes was evaluated by Jull et al. (129). Radiologically controlled diagnostic nerve blocks were used as the gold standard for this particular zygapophyseal joint syndrome. Physical examination methods to detect zygapophyseal joint dysfunction are active movement examination and manual passive segmental examination. This study demonstrated that the manual diagnosis, by a trained manipulative therapist, can be as accurate as can radiologically controlled diagnostic blocks. However, the authors conclude that further studies are required to validate the interobserver reliability.

The 'skin roll' test - pinching a fold of skin and subcutaneous tissue between the thumb and the other fingers, and rolling it forward across the surface - has been proposed by Maigne as a test for diagnosing the level of painful intervertebral dysfunction (9). Bansevicius and Pareja demonstrated that the 'skin roll' test, in a group of patients with CEH, migraine and tension-type headache, has not enough discriminative power to make it a reliable test for CEH (130). Jull et al. introduced a new test of cranio-cervical flexion which aims to assess impairment in the deep cervical flexor performance (124). The test demonstrated a significant different per-



formance of the deep flexors in CEH patients compared to the control group. Jull et al. concluded that this finding might have potential to identify musculoskeletal involvement in headache and may provide indications for manual therapy in CEH. The question arises whether these dysfunctions are primary causes of headache or merely epiphenomena. Pöhlmann showed in an overview that the results of manual diagnostic findings in the neck in patients with headache must be judged with caution due to heterogeneous and poorly defined study groups (70). Whether manual investigation has a role in the diagnosis of the various primary headache syndromes remain to be determined. Summarising the results of these studies in patients with CEH, it can be concluded that the majority is negative and that only the study from Jull et al. (124) may have a potential value.

### X-RAY INVESTIGATIONS

To exclude secondary causes of CEH, such as atlanto-axial subluxation due to rheumatoid arthritis, bone tumors etc., conventional X-ray examination of the cervical spine must be performed. The correlation between radiological degenerative changes, objectified by standard X-rays or magnetic resonance imaging (MRI), in the cervical spine do not correlate with pain (131-134). Fredriksen et al. did not find any abnormalities on standard X-ray of the cervical spine in patients with CEH (57). This is in concordance with the results of Pfaffenrath et al. (58). Extensive radiological examinations such as cerebral computed tomography (CT) scan, cerebral angiography and cervical myelography did not reveal abnormalities in patients with CEH (57). In a controlled study, Mayer et al. found a significant hypomobility in the C0/C1 or C0/C2 segment in patients with CEH by using a computer based analysis of functional radiographs in maximal flexion and extension (135). The diagnosis CEH was established in accordance with the clinical picture described by Sjaastad et al. and was confirmed by a positive diagnostic C2 block. Another study using a computer-based technique of analysis of cervical motion X-rays did reveal a statistically significant increase of upper cervical hypomobility and a reduction of general mobility from C0 to C5 in CEH patients as compared to controls (59). However, a segmental hypomobility in C0/C1 was also demonstrated in patients with tension-type headache and migraine (125). Bovim et al. showed that abnormal orbital phlebograms were equally frequent in cluster headache, migraine, tension-type headache and CEH (136). Vincent and Luna found also no particular changes on MRI scans of the cervical spine in patients with CEH (115). The 'ponticulus posticus' or foramen arcuale is a relatively common anatomic variation of the atlas and is considered by some authors as a causative factor in vertigo, Barré-Lieou syndrome and photophobia (137, 138). A recent study in a chiro-

practic patient population showed that there is no association between the existence of a 'ponticulus posticus', on the lateral X-ray and CEH (139). However, in this study the patients were not diagnosed according the criteria of Sjaastad et al. Up to now, no correlation was found between any (abnormal) radiological examination and patients with CEH. Functional MRI's and three-dimensional analysis can possibly provide more information on possible abnormalities in the cervical spine of CEH patients in the future.

## NEUROPHYSIOLOGICAL INVESTIGATIONS

Fredriksen and colleagues explored the possible involvement of the autonomic nervous system in CEH. Pupillometric tests in control subjects and patients with CEH were symmetric both during and between the headache attacks (56). In CEH patients a symmetrical forehead sweating was found during heating, exercise or pharmacological stimulation (55). In cluster headache patients, pilocarpine induces clearly more pronounced sweating on the symptomatic side compared with the non-symptomatic side (140). These experiments illustrated fundamental differences between CEH and cluster headache with respect to autonomic involvement.

Zwart and Sand demonstrated in a blinded study that the mean duration of the late exteroceptive suppression period of temporal muscle activity (ES2), a brainstem reflex, was similar in CEH, migraine, tension-type headache and controls (141). Consistent asymmetries of ES2 latency and duration in CEH patients were not present.

The eye blink reflex (BR) response is mediated via the trigeminal sensory afferent fibres and their central connections in the trigeminal nucleus (142). The R1 and R2 components of the blink reflex are useful in the diagnosis of trigeminal nerve disorders, facial nerve disorders, and brainstem dysfunction (143). The R1 and R2 components of the BR are mediated via tactile A $\beta$ -afferent fibres (144). The R3 components are probably mediated via thinly myelinated A $\delta$ -fibres (145). R1 and R2 blink reflex latencies were investigated blindly in 10 patients with CEH, 11 patients with chronic tension-type headache, 11 patients with migraine, and 9 headache-free controls (146). There were no R1 or R2 latency differences between the four groups. However, shorter R1 latencies were found on the symptomatic side than on the non-symptomatic side in CEH patients. The results may suggest that a state of hyperactivity may be present in the ipsilateral trigeminal nucleus in CEH. Although it has been suggested that the R3 may be useful in clinical pain diagnosis (145), its significance in CEH is not yet established.

Patients with CEH may complain of dizziness, a symptom hitherto not fully understood (13). In order to induce cervical dizziness as well as eye movement disturbances, Dieterich et al. carried out a study to deter-

mine eye-head-body co-ordination, using electronystagmography (ENG), subjective visual vertical test and posturography, before and after unilateral anaesthetic C2 block in CEH patients (147). They found that there is no clinical evidence for a significant influence of the C2 root on oculomotor or cerebellar function in patients with CEH.

CEH patients showed significantly higher electromyographic (EMG) amplitudes from the trapezius muscle on the symptomatic side, before and during the maximum voluntary contraction tests, compared with the non-symptomatic side (148). This was most pronounced during the test. These observations suggest a secondary muscular involvement in the pathogenesis of CEH according to the authors.

## DIFFERENTIAL DIAGNOSIS

Despite an apparent characteristic pattern of headache arising from the neck, there are still some difficulties in differential diagnosis, as there is some overlap of symptoms with other common primary headache syndromes. The differential diagnosis of CEH includes: 1) cluster headache; 2) hemicrania continua; 3) chronic paroxysmal hemicrania; 4) occipital neuralgia; 5) migraine; 6) tension-type headache. The main diagnostic problem in headache patients appears to distinguish CEH from migraine without aura and tension-type headache (70, 109).

### *Cluster headache*

The two major types of cluster headache are known as episodic and chronic. The episodic type is defined as periods of attack susceptibility, lasting an average of 1 to 3 months, followed by headache-free intervals (remission periods) of a few months to several years. Chronic cluster headache lacks remission periods, either from its inception (primary chronic) or after it has converted from the episodic type (secondary chronic).

The clinical picture of cluster headache is different from CEH. The mean duration of the attacks is 45 minutes, although they may last for 1-2 hours (23, 149). Attacks occur most commonly on relaxing after a day's work. Another common time for an attack is approximately 90 minutes after falling asleep, coinciding with the first REM state of sleep (150). The pain character of cluster headache is an extremely severe, constant, piercing pain. The pain of cluster headache is unilateral, almost always affecting the same side of the head in each bout, most commonly in and around the eye. It commonly radiates to the supra-orbital region, temple and maxilla on the same side. During the attack, which usually starts suddenly, the patient is not able to sit or lie-down quietly. Attacks are almost always associated with ipsilateral lacrimation, rhinorrhea or stuffiness and conjunctival suffusion. Ipsilateral ptosis and miosis are associated features found in a lesser number of patients. A provoking factor that is

consistently mentioned by patients is alcohol consumption during a bout. Other vasodilator substances such as histamine or drugs like nitroglycerine (used to prevent angina pectoris attacks), may precipitate an attack. Solomon et al. reported neck stiffness in 40% and tenderness in 29% of patients during an attack (151). In that study neck movements in 9% of the subjects could precipitate an attack.

Cluster headache affects men more frequently than women by a ratio ranging between 5:1 and 9:1 (23). A genetic role in the aetiology of cluster headache has been shown by Russel et al., who reported a 14 fold increase in the risk of cluster headache among first-degree relatives of a cluster population (152).

### *Hemicrania continua*

Hemicrania continua is a rare, indomethacin-responsive headache disorder characterised by a continuous, moderately severe, unilateral headache that varies in intensity, waxing and waning without disappearing completely (153). Hemicrania continua is not triggered by neck movements, but tender points in the neck may be present. Some patients may have photophobia, phonophobia and nausea. A positive therapeutic response to indomethacin can distinguish hemicrania continua from CEH. However, an indomethacin resistance have been described (154). Rothbart reported some borderline cases of CEH and hemicrania continua (155).

### *Chronic paroxysmal hemicrania*

Chronic paroxysmal hemicrania (CPH) was first described by Sjaastad and Dale in 1974 (155). Pain is strictly unilateral and without side shift in the majority of patients. The maximum pain is most often experienced in the ocular, temporal, maxillary and frontal region. Less often pain extends to the nuchal, occipital areas. The pain may occasionally radiate into the ipsilateral shoulder and arm. The pain is typically described as a throbbing, boring, pulsatile, sharp or stabbing sensation ranging from moderate to excruciating in severity (156). In CPH, attacks recur from one to forty times daily. Fluctuations in attack frequency have been documented. During episodes of headache, ipsilateral lacrimation, conjunctival injection, nasal congestion, or rhinorrhea may accompany the headache. Ipsilateral eye oedema, mild miosis, photophobia and nausea have been less frequently reported. CPH shows preponderance among women. No family history of CPH was found. CPH can occasionally be provoked by mechanical manoeuvres (157). Indomethacin is the treatment of choice for CPH. Responsiveness to indomethacin is an absolute diagnostic criterion for the diagnosis of CPH.

### *Occipital neuralgia*

The IHS classification defines occipital neuralgia as a paroxysmal, jabbing pain with diminished sensation or dysesthesia in the affected area as well as tenderness to palpation in the distribution of the greater or lesser occipital nerves (27). Some pain may persist between the paroxysmal attacks. The IHS insists that temporary relief by anaesthetic block is a diagnostic criterion. Paroxysmal lancinating pain is a key feature of neuralgia in general and is an essential diagnostic criterion for occipital neuralgia. Several authors report a considerable overlap of occipital neuralgia with migraine, tension-type headache and CEH (63, 158, 159).

### *Migraine without aura*

A main diagnostic problem is to distinguish CEH from migraine without aura (70, 109). CEH has some symptoms similar to migraine which can raise some difficulties in establishing the correct diagnosis (13, 53, 68, 160, 161). Both are unilateral headaches, affecting mainly females, and nausea, vomiting, phono- and/or photophobia may accompany them. These latter symptoms may be part of the clinical picture of CEH, but generally seem to occur less frequently and to be less outspoken than in migraine (13). Sjaastad has already addressed this problem in a series of papers (63, 65, 161-163). Clinical features to distinguish between the diagnosis of CEH and migraine are:

1. Unilateral headache without side shift is a major criterion in CEH but it may be present in 6.1-16.0 % of migraine patients (115, 162).
2. Mechanical triggering of headache is an obligatory criterion for CEH; it is reported not to occur in migraine patients (115). However, Blau et al report that 18% of migraine patients felt that the neck could act as a precipitant for some of their attacks (68).
3. Pain starting in the neck, eventually spreading to the oculofronto-temporal areas, where the maximum pain is usually located in CEH, while this happens in the minority of migraine patients.
4. The character of the pain in CEH is usually moderate, nonexcruciating and has a non-throbbing nature in stead of a throbbing-pulsating nature as in migraine (115).
5. Anaesthetic block of the greater occipital nerve and/or C2 root on the symptomatic side abolishes the pain transiently in CEH but not in migraine (115).

A characteristic of CEH is a headpain starting in the neck, eventually spreading to oculo-fronto-temporal areas where the maximum pain is often located. According to Blau et al., 14-20% of patients with migraine reports premonitory pain or stiffness in the neck (68, 164). Sjaastad et al, on the other hand found that in 12% of migraine patients the attack started in the neck or occiput (163). In the study of Vincent et al. this phenomenon was found in 6% of the migraine patients (115). In a logistic regression model Vincent et al. demonstrated that pain starting in the neck or occipital area was one of the most consistent differentiating factors between patients with CEH and migraine or tension-type headache. During or after the migraine attack neck pain was reported in up to 62% (68, 165). Headache starts in the oculo-fronto-temporal region in 75% of migraine without aura, 91% of migraine with aura, but in 17% of CEH (65, 163).

The differential diagnosis in unilateral and persistently lateralised migraine attacks may pose an unresolvable dilemma in 16-21% of patients (162, 166, 167). Applying migraine criteria to CEH patients reveals that 20-30% met the IHS criteria for migraine which is relatively high (115, 162). However, application of the above-mentioned criteria (1-5), which are typical for CEH, will allow a better differentiation between migraine and CEH. According to Vincent and Luna, the best differentiating criteria for migraine and CEH were: 1) unilaterality without sideshift; 2) pain starting in the neck, eventually radiating to the frontal area; 3) similar pain triggered by neck movement and/or sustained awkward position (115). Although the diagnosis can be difficult to establish in the individual patient, it is not the presence of a single criterion but a set of criteria that leads to the diagnosis.

### *Tension-type headache*

The character of CEH may present as a mild, non-throbbing, episodic pain, which can resemble tension-type headache. With regard to two important IHS criteria such as a pressing quality and no aggravation by physical routine activity, Vincent et al. found no differences between tension-type headache and CEH (115). Bilateral localisation of the headache and the absence of mechanical trigger factors, in the majority of tension-type headache patients, allow differentiation between tension-type headache and CEH (168). In 10.3% of patients with tension-type headache, the headache was triggered by neck movement or sustained awkward head position and in 6.9% of the patients the pain was elicited by external pressure over the ipsilateral neck or occipital region (115).

Bilateral cases of CEH can complicate the distinction with tension-type headache (63). Using the IHS criteria, only one CEH patient would be diagnosed as having tension-type headache (115).

## THERAPY

Conservative treatment is the cornerstone of therapy in all headaches, although invasive treatment might be an option for some particular headache syndromes. Therapies in heterogeneous groups with a broad spectrum of complaints and a vague diagnosis will only contribute to controversy surrounding the value of different treatment modalities for CEH. Therefore, in this review only therapies for CEH, based on the criteria of Sjaastad et al. or the IHS that result in a clear and reliable diagnosis, will be evaluated.

Conservative treatment contains several modalities such as 1) pharmacological treatment; 2) manual therapy; 3) transcutaneous electrical nerve stimulation (TENS). If conservative treatment does not provide any substantial pain relief, invasive procedures may be of benefit.

### *Pharmacological treatment*

Patients with CEH often use simple analgesics, like paracetamol (acetaminophen) and nonsteroidal anti-inflammatory drugs (NSAIDs). In the majority of patients these drugs give only a transient relief of the headache and according to many patients the effect decreases over time. There are no convincing clinical studies to determine the efficacy of paracetamol and NSAIDs. Because both paracetamol and NSAIDs are often acquired in over-the-counter preparations, exact figures about the efficacy of these drugs are missing. Drugs like morphine have only a marginal effect and are generally not indicated to be prescribed to CEH patients (169). Unlike cluster headache, ergotamine or oxygen inhalation are not effective in CEH (169). Instead of diminishing headache complaints, nitroglycerine, a (venous) vasodilator, increases the headache in patients with CEH (169). The efficacy of the new 5-HT<sub>1D</sub> receptor agonists needs to be established in CEH. To exclude hemicrania continua, a short course of indomethacin can be prescribed to the patient.

### *Manual therapy (spinal manipulation and mobilisation)*

Spinal manipulation is used extensively in the treatment of headaches with symptomatic spinal segmental joint or dysfunction (170-176). The technique of treatment is based on detailed manual examination. This manual examination, the so-called segmental spine examination, is performed to identify the precise localisation of segmental dysfunction(s) and tenderness. Many techniques can be used at one or more segments. Spinal manipulation uses short high velocity with low amplitude thrusts directed to one or more segment(s) in the cervical spine. By means of specific holds it is possible to mobilise hypomobile segments. Mobilisation consists of soft passive movement of the segment at the outer range of motion. In muscle energy technique the treatment is started



by an isometric muscle contraction performed by the patient in the opposite direction to the manual treatment (177).

Only few spinal manipulation trials have been performed to show its efficacy in headache and CEH. Whittingham et al. performed a pilot study to investigate the effect of spinal manipulation in 26 patients with chronic unilateral headache of cervical origin (Table 2) (122). Physical examination revealed upper cervical joint dysfunction in all patients. He used the toggle recoil technique to treat the upper two cervical vertebrae of the patients. He found a significant reduction in headache frequency, duration and intensity in the majority of the patients and concluded that a randomised controlled trial is needed to establish the efficacy of spinal manipulation. In another uncontrolled study of 10 patients with headache of cervical origin, mobilisation of the upper cervical spine resulted in a decrease in headache frequency, duration and intensity (Table 2) (175). However, in the short follow-up period (4-8 weeks) a worsening of some variables was found. A flaw in both studies was that the patients were not selected according to the criteria from Sjaastad et al. or the IHS classification, which resulted in inhomogeneous groups.

In 1995, Nilsson et al. conducted a randomised controlled trial with a blind observer on the effect of spinal manipulation in the treatment for CEH (Table 2) (178). Thirty-nine CEH patients, fulfilling IHS classification criteria, were included in this prospective study. The 'active treatment' group received high-velocity, low amplitude cervical manipulation while the 'control' group received low-level laser therapy in the upper cervical region and deep friction massage in the lower cervical area. In this study no significant reduction in the duration of the headache, headache intensity and analgesic consumption was found in comparison with the control group. Nilsson suggested that this failure might well be due to methodological problems such as a relatively small number of patients. Therefore, he decided to resume the recruitment of patients with CEH into the same trial resulting in a two period recruitment approximately 1 year apart (179). This serial study showed a significant positive effect in all three variables in subjects with CEH. However, the results were obtained one week after the last therapy session and a longer follow-up period will be needed to establish the efficacy of spinal manipulation in CEH.

Although there is some risk for cervical spinal manipulation, the prevalence is extremely low (180, 181).

### *TENS therapy*

Introduction of the gate control theory concept in 1965 has facilitated the development of afferent stimulation techniques for alleviation of pain, such as TENS (182). The application of TENS as a pain-relieving method is by far the most extensively used biomedical technique for various painful conditions including tension-type headache. Headache and TENS



**Table 2. Results manual therapy in patients with CEH.**

Author	Patients	Diagnosis	Design
Whittingham et al. 1994	26	Headache <sup>(c)</sup>	C
Schoensee et al. 1995	10	Headache <sup>(c)</sup>	C
Nilsson et al. 1995	39	CEH <sup>(b)</sup>	A
Nilsson et al. 1997	53	CEH <sup>(b)</sup>	A

*Diagnosis:*

<sup>(a)</sup> diagnosis CEH according Sjaastad's et al criteria, homogeneous group of patients

<sup>(b)</sup> diagnosis CEH according IHS classification, homogeneous group

<sup>(c)</sup> unilateral headache and neck pain, heterogeneous group of patients

<sup>(d)</sup> headache and neck pain, heterogeneous group of patients

*Design of the study:*

A: double-blind randomised trial (RCT)

B: Observational prospective study with control group

C: Observational prospective study without control group

D: Observational retrospective study without control group

Treatment	Results	Follow-up
Toggle recoil adjustments in upper cervical spine	92% of patients significant reduction in headache frequency, duration and severity	2 weeks
Mobilisation in upper cervical spine	Decrease in headache frequency, duration and intensity	4 weeks
High-velocity, low-amplitude cervical manipulation	No significant results	1 week
High-velocity, low-amplitude cervical manipulation	71% of patients significant reduction in headache duration, intensity and analgesic consumption	1 week

therapy is employed by several authors (50, 183-187). The studies by Airaksinen and Pontinen (187) and Solomon and Guglielmo (183) involved only patients with tension-type headache. Airaksinen and Pontinen investigated the short-term changes in pressure pain threshold at trigger points in patients with tension-type headache and found a significant increase in pain thresholds (187). Another study investigated the prophylactic benefit of TENS in patients with tension-type headache and found that TENS is more efficacious than placebo (183). Farina et al. applied TENS therapy in 10 patients with CEH, 15 patients with occipital neuralgia, and 35 patients with mixed headache (184). Assessment was performed before and after the treatment. This study demonstrated that TENS is effective in 70-80% of patients in all three groups. A randomised clinical trial in patients with CEH was performed by Tarhan and Inan (50). They found a significant improvement in the treatment group after 3 months compared to a placebo group. However, due to the nature of the method, realistic placebo and blinding are inherent problems in TENS studies (188, 189). Therefore, the results must be interpreted with caution.

### *Invasive therapy*

Local anaesthetic blocks of the greater occipital nerve (GON) are frequently used in the diagnostic work-up in CEH patients. Besides as a diagnostic tool, injections with a local anaesthetic at the GON are also used as therapy. Vincent et al. demonstrated in a subgroup of patients (Visual Analogue Scale less than 40 mm.) with CEH a significant relief of headache complaints during seven days after infiltration around the GON with bupivacaine 0.5% 1-2 ml (Table 3) (190). Anthony suggests that the results of repeated local injections of an anaesthetic solution around the GON may be more favourable by combining it with corticosteroids (191). Nevertheless, only in isolated cases was long lasting headache relief achieved by local injection therapy (58). Up to now, it should not be considered as a permanent treatment modality.

Jansen et al. selected a group of 11 patients suffering from severe hemicranial attacks who underwent a neurosurgical operation (192). In 9 of the 11 patients a vascular compression due to varicose veins (n=7) or arterial loops (n=2) of the C2 root was found at operation. Aim of the operation was to release the nerve roots from vascular compression. The post-operative results were good (Table 3) with a recurrence of head pain in 2 patients who were further treated by a percutaneous radiofrequency (RF) lesion of the dorsal root ganglion C2, where upon 1 patient became pain free.

Pikus and Philips performed a similar study (193). They operated 35 patients with CEH and performed 39 decompressions of the C2 root and ganglion. Bilateral decompression was accomplished in 4 patients. Their retrospectively analysed results were good at a mean follow-up of 21 months (Table 3). Recurrence of symptoms was reported in 21% of pa-

tients at an average follow-up of 18 months. Patients who had a recurrence of symptoms or in whom the first operation eventually failed underwent re-operation(s). The final outcome (either pain free or with adequate improvement) after a second or third operation was 89%. In their study no patient was worse after surgical intervention. They decompressed the C2 root and ganglion by removal of ligamentous structures and venous structures. During such operation electro-cautery of (small) vessels is essential because the C2 ganglion is normally situated amidst an impressive venous plexus. Therefore, Stechinson suggests that traumatising the C2 by electro-cautery may explain their results (194). He also questioned their hypothesis regarding the vascular compression of the dorsal root ganglion as the cause of the pain. In their study no specific prognostic factors could be established to directly select patients amenable to C2 root and ganglion decompression (195).

Entrapment of the GON in its peripheral course is considered as a possible pathogenic mechanism for CEH (196). Bovim et al. suggested that a neurolysis of the GON in the nuchal musculature, with special interest at the point where the GON penetrated the trapezius muscle, might be a beneficial therapy (196). He studied this in an uncontrolled trial with 50 patients. Although the initial results were quite good, the head pain gradually recurred in the majority of patients after a follow-up period of one-year (Table 3). Therefore, they advocate that this liberation operation at the GON should not be performed in patients with CEH.

Injection of intracutaneous sterile water has been reported, in an open uncontrolled study, to be effective in patients with neck pain after a whiplash trauma (197). In a double-blind cross-over design study (using sterile water and isotonic saline) the authors demonstrated that injection of sterile water was not effective in CEH patients (Table 3). Not even a slight positive trend was demonstrated. Nevertheless, the probability remains that the mechanism of pain in post whiplash syndrome may be different from CEH.

Martelletti et al. aimed to assess the short-term efficacy of cervical epidural corticosteroids in nine patients with CEH diagnosed according to the criteria from Sjaastad et al. (198). The control group consisted of six patients with tension-type headache who underwent a cervical epidural injection with 40 mg. methylprednisolone in 3-4 ml. saline. The short-term results (1 month) revealed significantly lowered Numeric Pain Intensity Scales in the CEH group compared with the control group (Table 3). However, during the follow-up a progressive clinical worsening was established in the CEH group indicating that cervical epidural injection with corticosteroids has no place in the therapeutic arsenal (199).

Radiofrequency (RF) lesions have been proved to be beneficial in different pain syndromes (204-207). RF-lesions are controllable heat lesions used to reduce nociceptive input (200-202). It is theorised that CEH

**Table 3. Results invasive treatment in patients with CEH.**

Author	Patients	Diagnosis	Design
Jansen et al. 1989	11	CEH <sup>(c)</sup>	C
Bovim et al., 1992	50	CEH <sup>(a)</sup>	C
Sand et al., 1992	10	CEH <sup>(a)</sup>	A
Sjaastad et al. 1995	7	CEH <sup>(a)</sup>	C
Pikus and Philips 1995	35	CEH <sup>(a)</sup>	D
Martelletti et al. 1998	12	CEH <sup>(a)</sup>	B
Van Suijlekom et al. 1998	15	CEH <sup>(a)</sup>	C
Vincent et al. 1998	41	CEH <sup>(a)</sup>	C
Jansen et al., 1999	8	CEH <sup>(b)</sup>	C
Freund et al., 2000	26	CEH <sup>(a)</sup>	A *

*Diagnosis:*

*(a)* diagnosis CEH according Sjaastad's et al criteria, homogeneous group of patients

*(b)* diagnosis CEH descriptive, heterogeneous group

*(c)* diagnosis CEH according IHS criteria, heterogeneous group

*Design of the study:*

A: double-blind randomised controlled trial (RCT)

B: Observational prospective study with control group

C: Observational prospective study without control group

D: Observational retrospective study without control group

\* groups are not comparable

Treatment	Results	Follow-up
vascular decompression C <sub>2</sub>	77% pain free, 23% improved, 23% recurrence	27.0 (4-125) months
neurolysis of GON	46% pain free, 36% some relief 8% pain free	1 week 16 months
intracutaneous sterile water injection in tender points	0% improved	13 days
Frontal treatment planum nuchale	42% pain free, 29% improvement	4.5 years
Microsurgical decompression of ganglion C <sub>2</sub> (first operation)	33% pain free, 46% improved	21 (3-70) months
Oral corticosteroids	Good improvement No improvement	1 month 6 months
Radiofrequency neurotomy of dorsal ramus C <sub>3</sub> -C <sub>6</sub> (facet joint)	80% complete/good relief 64% complete/good relief	8.8 (4-14) months 16.8 (12-22) months
GON block with local anaesthetic	Significant improvement in VAS score	7 days
Unilateral cervical laminotomy and laminoplasty	38% pain free, 38% improvement	2.5 (2-3) months
Botulinum toxin A injection in muscular cervical triggerpoints	Significant improvement in VAS score	4 weeks

might be the result of an aberrant nociceptive input from different sources in the neck onto the central nervous system (50, 203). Therefore, reducing some of this input may decrease the headache in CEH. Various structures in the neck, such as the zygapophyseal joints, intervertebral discs, dorsal root ganglia, muscles and ligaments, are capable of causing neck pain and headache (49, 53, 81, 110, 128). The zygapophyseal joints of the cervical spine are recognised as important pain producing structures in headache (208). Of all aforementioned cervical structures, the zygapophyseal joints are probably the most accessible targets for invasive therapy. In particular, cervical zygapophyseal joint neurotomy by radiofrequency is a procedure which is generally easy to control and which has no clinically recognisable side effects. Therefore, we performed a prospective open study in 15 patients with CEH in order to assess the clinical efficacy of radiofrequency cervical zygapophyseal joint neurotomy (Table 3) (209). The study demonstrated good results after long-term follow-up (mean 16.8 months). The efficacy of this treatment appears to be maximal in the 4-14 months (mean 8.8) after treatment, with a tendency of some variables to worsen gradually in the long-term follow-up period. Side effects were minimal using this minimally invasive technique. Since the results of this study were not adequately controlled they cannot be seen as a definitive proof supporting the clinical efficacy of radiofrequency zygapophyseal joint neurotomy for CEH. Therefore, a definitive conclusion about the clinical efficacy of the procedure can only be drawn from a randomised controlled trial.

Sjaastad et al. selected a group of 7 patients with CEH who underwent percutaneous RF treatment of the periosteum of the external surface of the occipital bone (planum nuchale) on the symptomatic side (210). This technique was described by Blume in patients with persistent myalgia-neuralgia syndrome (10). In 5 (71%) patients from Sjaastad's study, an improvement of varying degree was obtained after a follow-up of 4.5 years (Table 3). In one patient, who did not improve, a local effusion in the operated area was developed in the post-operative course after 10 days, which continued for approximately 2 months.

Injection of botulinum toxin into localised tender areas of the left trapezius muscle has been reported successfully in a patient with unilateral headache after a whiplash injury (211). Freund et al. performed a randomised double-blind, placebo controlled study in 26 subjects with chronic headache secondary to a whiplash injury (212). The subjects, 11 men and 15 women with unilateral and bilateral headache, met all major and characteristic diagnostic criteria from Sjaastad et al. with the exception of a positive diagnostic anaesthetic block. The treatment group received 100 units botulinum toxin A in cervical triggerpoints. Follow-up during 2 and 4 weeks after injection demonstrated a significant improvement in pain and range of motion from pre-injection levels (Table 3).

However, the treatment and control group were not comparable because statistically significant difference in pre-injection (head) pain was present. Unfortunately the follow-up period was 4 weeks.

In 1999, Jansen reported the results of dorsal decompressive laminotomy and laminoplasty in the cervical spine in 8 patients with headache originating from the neck (203). These patients were operated only after a positive segmental epidural anaesthetic block (213). Seven patients suffered from a bilateral headache stemming from the neck. The results in this study were good (Table 3). However, the follow-up in this study was too short (2.5 months) to conclude whether this treatment is a therapy of choice in a selected group of patients. Jansen suggests that the dura mater, with its nociceptive nerve fibres, might be an important trigger mechanism for CEH in some patients.

To conclude, several of the above mentioned trials show positive results that range between fair to quite good. However, nowadays it is standard in medicine to assess the clinical efficacy of a therapy only by a randomised controlled study design. Only two randomised controlled trials are performed in patients with CEH (197,212). Reviewing the invasive studies, with a broad spectrum of treatment modalities, it is difficult to distill a preferable sequence of treatment. However, when the weight of the 'operation' is involved in the process of treatment choice, a sequence of preference can be determined from low invasive to highly invasive therapy.

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$$= \frac{2}{3} \pi \times 10^{-21} \text{ cm}^3$$

For  $\rho = 0.14 \text{ g cm}^{-3}$ ,  $\mu = 0.001 \text{ cm}^2 \text{ g}^{-1}$  and  $\lambda = 0.0001 \text{ cm}$  the  
 average  $\mu$  is  $0.001 \text{ cm}^2 \text{ g}^{-1}$  and  $\lambda = 0.0001 \text{ cm}$ .



## CHAPTER 3

### **Interobserver reliability of diagnostic criteria for cervicogenic headache**

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## ABSTRACT

To assess the interobserver reliability in distinguishing cervicogenic headache (CEH) from migraine without aura and tension-type headache we conducted a study which approached daily clinical practice as close as possible. In contrast to other reliability studies, which used data from clinical patient records or semi-structured interviews recorded on videotape ('in vitro' design), we examined 'live' patients ('in vivo' design). Twenty-four headache patients participated in our 'in vivo' design experiment. During a session each physician queried six patients in succession using a semi-structured interview and performed a physical examination. Diagnosis was made according to the IHS criteria and the criteria from Sjaastad and co-workers. Kappa statistics were used, being kappa = 0.83 between the expert headache neurologists; kappa = 0.74/0.73 between the expert anaesthesiologist in (head) pain treatment and both expert neurologists respectively; kappa ranged from 0.43 – 0.62 between the other physicians. The results of our 'in vivo' design study showed that the reliability in diagnosing CEH, when strictly applying the criteria from Sjaastad and co-workers, is similar to the reliability in diagnosing migraine and tension-type headache according to the IHS criteria.

**Keywords:** Cervicogenic headache, interobserver reliability, kappa statistics, migraine, tension-type headache

## INTRODUCTION

Cervicogenic headache (CEH) is a clinically defined headache syndrome which is hypothesised to originate from nociceptive structures in the cervical spine. Barré used the term 'syndrome sympathique cervicale supérieur', and Bärtschi-Rochaix introduced the term 'migraine cervicale' for headaches that might originate from the cervical spine (1, 2). However, despite its long history, the concept of CEH is still controversial (3, 4). In an effort to standardise research in CEH Sjaastad and co-workers in 1990 published criteria for the diagnosis (5), with a recent revision in 1998, summarised in Table 1 (6).

The headache classification by the International Headache Society (IHS) (7) has been shown to provide satisfactory interobserver reliability for the diagnosis of primary headaches (8, 9). CEH is still not admitted as a separate primary headache syndrome into the IHS classification, hence reliability of the CEH criteria has not been studied in the IHS reliability experiments. In contrast, the International Association for the Study of Pain (IASP) classification does include CEH (10). The main diagnostic problem in headache patients is to distinguish CEH from migraine without aura and tension-type headache (11, 12). Vincent et al. compared CEH with migraine and tension-type headache (13). In their prospective study, using data from patient records, these authors showed that, using the Sjaastad and co-workers 1990 criteria (5), CEH clearly differs from migraine and tension-type headache and that the existing criteria seem to be adequate for distinguishing between them.

It is important to realise that all these reliability studies represented an 'in vitro' experiment, i.e. reaching a headache diagnosis from written data in a patient record and thus focussing on the reliable application of the criteria. The principal question thus remains as to the interobserver agreement in applying the CEH criteria when examining 'live' patients ('in vivo' study design) including the variance in response of patients when asked about their complaints and examined for their symptoms.

The objective of our study was to assess interobserver agreement in distinguishing CEH from migraine without aura and tension-type headache, when different physicians examine 'live' headache patients as in routine daily clinical practice. In the present study of 6 physicians examining 24 headache patients, it will be shown that the interobserver reliability in diagnosing CEH is similar to that of variability in diagnosing migraine and tension-type headache.

## PATIENTS AND METHODS

Twenty-four patients, 11 females and 13 males, mean age 43 years (range 29-59), were included in the study. Only patients diagnosed as migraine without aura, tension type headache or CEH were included in this study. The patients, diagnosed as migraine without aura or tension-type headache according the IHS criteria, were selected at random from the computerised headache patient database of the department of neurology of the University Hospital of Maastricht. All patients with tension-type headache appeared to have bilateral complaints. Although unilateral tension-type headache has been reported, it appears to be a very small minority of patients (14). Our patient sample thus appears to be representative for daily clinical practice. Patients with putative CEH, referred by neurologists to the Pain Management and Research Centre, were consecutively selected. Although bilateral CEH has been reported, the CEH criteria guidelines strongly advise to include only unilateral cases for research purposes (6). At each session, involving 6 patients, we intended to have 2 putative CEH patients mixed up with 2 patients diagnosed as migraine and 2 patients with tension-type headache. Blindings procedures were guaranteed.

The study was set up in four (I-IV) sessions with six patients and six physicians at each session. Our study intended to encompass the two medical disciplines which are involved in the diagnosis and treatment of CEH. In the Netherlands invasive treatment for CEH is done by anaesthesiologists (15). At each session, two expert headache neurologists (N+), two general neurologists (N) and two anaesthesiologists (A), were scheduled to be present. One anaesthesiologist (4A) who participates in the study is an expert in pain treatment and one anaesthesiologist (5A+) is an expert in (head) pain treatment. The intention was to have the same physicians at each session during the study period. During three sessions (I, III, IV) we have had the same five physicians with one locum tenens. In one session (II) three physicians countermanded and were replaced by three other physicians with the same expertise. All the physicians were familiar with the different headache disorders.

Each patient was queried by six physicians using a semi-structured interview. A semi-structured interview is the most practical method to obtain information used in formulating the diagnosis (16). This semi-structured interview has been prepared by the investigators and a panel of experts in the headache field, and comprised all the information required to make the correct diagnosis of migraine and tension type headache according to the IHS criteria (7) and CEH according to the criteria of Sjaastad et al.(6). Each question was coded as yes/no, e.g. my headache can be precipitated by neck movement and/or sustained awkward positioning of my head. Although the questions were structured, the interviewer was free to

ask successive questions to ensure the accuracy of information. At the end of the interview a physical examination of the cervical spine was performed.

Physical examination of the cervical spine consisted of several items: a) functional examination of the cervical spine assessing restriction of the range of motion; b) provocation of the head pain similar to the spontaneously occurring one by external pressure over the upper cervical or occipital region on the symptomatic side. All these items were scored with yes/no. After each interview and physical examination, physicians were asked to give their diagnosis of the headache i.e. 1) CEH according to the criteria from Sjaastad and co-workers (6) or 2) migraine or 3) tension-type headache or 4) other headache according the IHS (7).

Whenever a patient seems to have two separate types of headache the physicians were instructed to check off these various headache types, in different columns, at the same questionnaire resulting in 2 headache diagnoses in one patient.

Requirements for the diagnosis of CEH are the presence of point Ia, and III; or the combination of Ib, Ic and III. Presence of other points, see Table I, also further supports the diagnosis (6). In this study point II i.e. confirmatory evidence by diagnostic anaesthetic blockades, was not performed. It is methodologically difficult (probably impossible) to test diagnostic nerve blocks in an identical experiment in order to assess clinical reliability. Six diagnostic nerve blocks cannot be performed in one patient in one session without interpretation difficulties being encountered.

Interobserver agreement on the types of headache was assessed by calculation of kappa statistics (17). Kappa is the most adequate measure, for interobserver agreement and kappa adjusts the observed agreement for chance agreement (17). Kappa values range from -1 to 1, with 0 representing only chance agreement. Positive values show certain agreement beyond chance agreement. Besides measurement of kappa values between pairs of observers, we also measured a group kappa. In the group kappa coefficient, the average observed agreement is compared to the average chance agreement, with the average taken over all pairs of observers and over all patients.

## RESULTS

### *Interobserver agreement: headache diagnosis.*

The kappa values for final headache diagnosis between the different pairs of observers ranged from 0.43 to 0.83 (Table 2). Interobserver agreement between the expert headache neurologists was 0.83, while the agreement between the general neurologist (3N) and the expert headache

**Table 1. Criteria for cervicogenic headache.**

**MAJOR CRITERIA**

**I. Symptoms and signs of neck involvement:**

- a) Provocation of an irradiating head pain, similar to the spontaneously occurring one:
  - 3) By neck movement and/or sustained, awkward head positioning, and/or
  - 4) By external pressure over the upper cervical or occipital region on the symptomatic side.

- b) Restriction of the range of motion (ROM) in the neck

- d) Ipsilateral neck, shoulder, or arm pain of a rather vague, nonradicular nature, or – occasionally – arm pain of a radicular nature

**II. Confirmatory evidence by diagnostic anaesthetic blocks.**

**III. Unilaterality of the head pain, without sideshift.**

**PAIN CHARACTERISTICS**

**IV. Non-throbbing pain, usually starting in the neck**

Episodes of varying duration, or

Fluctuating, continuous pain

**OTHER CHARACTERISTICS**

**IV. Only marginal effect or lack of indomethacin.**

Only marginal effect or lack of effect of ergotamine and sumatriptan.

A certain female preponderance.

Head or indirect neck trauma by history, usually of more than only medium severity

**OTHER DESCRIPTIONS OF LESSER IMPORTANCE**

**V. Various attack-related phenomena, only rarely present, and/or moderately expressed when present.**

g) Nausea

h) Phonophobia and photophobia

i) Dizziness

j) Ipsilateral 'blurred vision'

k) Difficulties on swallowing

l) Ipsilateral edema, mostly in the periocular area

neurologists (1N+, 2N+) were 0.43 and 0.43 respectively. The kappa values between the anaesthesiologists (4A and 5A+) and the neurologists headache experts (1N+ and 2N+) were 0.50/0.49 and 0.74/0.73 respectively. Kappa values between the general neurologist (3N) and the two anaesthesiologists (4A and 5A+) were 0.62 and 0.55 respectively. Among the two anaesthesiologists (4A and 5A+) the kappa value was 0.55. The overall group kappa value for the agreement between the 9 observers and

24 patients was 0.51 (CI: 0.36-0.66). The agreement in the headache diagnoses assessed by 5 observers who all examined the same 18 patients (session I, III and IV) showed a group kappa of 0.56 (CI: 0.38-0.73).

Table 2. Kappa values for agreement between pairs of observers.

Observer	1 (N+)	2(N+)	3(N)	4(A)	5(A+)
1(N+)					
2(N+)	0.83				
3(N)	0.43	0.43			
4(A)	0.50	0.49	0.62		
5(A+)	0.74	0.73	0.56	0.55	

(N+) = expert headache neurologist

(N) = general neurologist

(A) = expert anaesthesiologist in pain treatment

(A+) = expert anaesthesiologist in head pain treatment

In 5 patients a second type of headache was diagnosed by several physicians. Patient no. 4, 8 and 9 were diagnosed as having migraine too by 3, 2 and 3 physicians respectively while this was not once the primary headache diagnosis. Two physicians diagnosed patient no. 13 as having tension-type headache as a separate second headache, while 2 physicians diagnosed tension-type headache as the primary headache. In patient no. 14 tension-type headache and CEH was diagnosed by 3 and 2 physicians respectively while migraine was unanimously the primary diagnosis.

In order to assess which headache is most difficult to distinguish from the others we performed a frequency distribution of the headache diagnoses (Table 3). The second column from the left shows the combined frequency distribution of the scores of the observers (n=144). The rows show the frequency distribution of the other physicians, when one physician assigned the diagnosis in the left-hand column. When the patients were diagnosed as migraine by one physician, the distribution of the other headaches was 11% tension type headache, 11% CEH and 1% other headache. For patients who were diagnosed as having CEH by one physician, the distribution of the others was 8% migraine, 13% tension type headache and 3% other headache. These frequency distributions demonstrated that migraine as well as CEH, using the existing criteria, could be distinguished adequately from each other. For patients diagnosed as tension type headache by one physician, the distribution of the others was 17% migraine, 28% CEH and 10% other headache. This means that in our experiment tension-type headache is most difficult to distinguish from the other headaches.

**Table 3. Frequency distribution (%) on the scores of 24 patients, conditional on the judgement of the other observers.**

	Total scores (n=144)	Migraine	Tension-Type headache	Cervicogenic headache	Other headache
Migraine	44	77%	11%	11%	1%
Tension-Type headache	29	17%	45%	28%	10%
Cervicogenic headache	64	8%	13%	76%	3%
Other headache	7	9%	43%	31%	17%

***Observer agreement: items in the headache history.***

Findings of observer agreement of the whole group for each history item relevant to reach a headache diagnosis are summarised in Table 4. The kappa scores for the several items vary from 0.08 – 0.76 indicating that some questions cannot be assessed unequivocally. The kappa scores of the major criteria of CEH (items 1, 3, 4, 5, 6), differentiating this syndrome from migraine and tension-type headache, ranged between 0.45 – 0.76, indicating moderate to substantial agreement.

***Observer agreement: items in physical examination.***

Items for physical examination at the cervical spine regarding the major criteria of CEH are shown in Table 5. Assessment of a restriction of the range of motion in all patients revealed kappa scores between 0.32 – 0.41, indicating only fair to moderate agreement. Provocation of the head pain similar to the usually occurring one by movements of the neck varied between 0.53 – 0.59 which implies a moderate agreement. Elicitation of the headache by manual pressure against the cervical zygapophyseal joints ranged between 0.16 – 0.23 which indicates only a slight to fair agreement. Other areas from which the headache may be precipitated, are 1) along the greater occipital nerve; 2) the groove immediately behind the mastoid process; 3) the upper part of the sternocleidomastoid muscle which probably corresponds to the minor occipital nerve(6). These areas show kappa scores ranging between 0.21 – 0.31, which are also slight to fair.

## DISCUSSION

To our knowledge this study is the first 'in vivo' based experiment to assess the interobserver agreement in diagnosing CEH. This design closely resembles the diagnostic process in daily patient care. Reliability of diagnosis not only means that the clinical symptoms are interpreted in a reproducible way but also that the symptoms are expressed in a reliable

**Table 4. Group kappa values per question.**

Question	Kappa value	95% CI
1. The headache is always localised on 1 side of the head.	0.46	(0.26-0.66)
2. The headache is localised bilateral.	0.50	(0.32-0.69)
3. The pain starts in the neck, with radiation to the fronto-temporal region.	0.67	(0.50-0.84)
4. The pain radiates to the ipsilateral shoulder and arm.	0.76	(0.60-0.91)
5. The patient says that the headache is provoked by neck movements.	0.45	(0.22-0.68)
6. The patient says that the range of motion in the neck is impaired.	0.54	(0.34-0.74)
7. The headache is of a nagging, non-throbbing character.	0.51	(0.28-0.75)
8. The headache is of a tight, pressing, non-pulsatile character (non-throbbing).	0.43	(0.20-0.66)
9. The headache has a throbbing character.	0.65	(0.45-0.85)
10. The headache episode takes about 4-72 hours.	0.48	(0.27-0.68)
11. The headache episode takes about 30 minutes to 7 days.	0.08	(0.01-0.16)
12. The headache episode is various from 1-14 days.	0.26	(0.02-0.49)
13. The intensity is mild.	0.29	(0.03-0.55)
14. The intensity is mild to severe.	0.20	(0.04-0.36)
15. The intensity is very severe.	0.42	(0.20-0.65)
16. Physical activity leads to a increase of the pain.	0.24	(0.08-0.40)
17. Nausea.	0.70	(0.49-0.89)
18. Vomiting.	0.62	(0.33-0.90)
19. Photo-phobia.	0.69	(0.50-0.87)
20. Phono-phobia.	0.68	(0.47-0.89)
21. Dizziness.	0.72	(0.52-0.92)
22. Autonomic features (conjunctival injection, lacrimation, nasal congestion, rhinorrhea etc.)	0.40	(0.13-0.67)
23. Aura.	0.36	(0.23-0.49)

way. Other studies used clinical records or structured interviews recorded on videotape and focussed only on the reliable application of the criteria (8, 9, 18, 19). The above mentioned headache reliability studies used kappa statistics as a measure of interobserver agreement. According to Landis and Koch (20) kappa values are classified as indicating slight (kappa = 0.00-0.20), fair (kappa = 0.21-0.40), moderate (kappa = 0.41-0.60), substantial (kappa = 0.61-0.80) and almost perfect agreement (kappa = 0.81- 1.0). Terms such as reliability, (interobserver) agreement and reproducibility are concepts that mean the same.

In our study we used kappa as a measure of interobserver agreement, both for the whole group (overall agreement) as well as for each



**Table 5. Group kappa values per item regarding physical examination at the cervical spine.**

Item of physical examination	Kappa value	95% CI
1. Restricted range of motion: flexion	0.32	(0.11-0.53)
2. Restricted range of motion: retroflexion	0.32	(0.16-0.48)
3. Restricted range of motion: rotation right	0.39	(0.21-0.57)
4. Restricted range of motion: rotation left	0.41	(0.22-0.59)
5. Items 1-4 combined	0.33	(0.13-0.52)
6. Pain provocation flexion	0.55	(0.34-0.75)
7. Pain provocation retroflexion	0.59	(0.39-0.80)
8. Pain provocation rotation right	0.57	(0.38-0.77)
9. Pain provocation rotation left	0.53	(0.32-0.73)
10. Items 6-9 combined	0.51	(0.29-0.74)
11. High zygapophyseal pressure pain	0.23	(0.09-0.36)
12. Mid zygapophyseal pressure pain	0.21	(0.04-0.37)
13. Low zygapophyseal pressure pain	0.16	(0.01-0.31)
14. Pressure pain occiput left (GON) <sup>1</sup>	0.26	(0.11-0.41)
15. Pressure pain occiput right (GON) <sup>1</sup>	0.26	(0.09-0.43)
16. Pressure pain mastoid left	0.33	(0.10-0.55)
17. Pressure pain mastoid right	0.24	(0.08-0.41)
18. Pressure pain insertion m.SCM <sup>2</sup> on occiput left (MON) <sup>3</sup>	0.21	(0.05-0.36)
19. Pressure pain insertion m.SCM <sup>2</sup> on occiput right (MON) <sup>3</sup>	0.32	(0.15-0.48)

<sup>1</sup> GON = Greater Occipital Nerve

<sup>2</sup> m.SCM = musculus sternocleidomastoideus

<sup>3</sup> MON = Minor Occipital Nerve

pair of observers (Table 2). The overall agreement was moderate (kappa = 0.51). Lack of agreement in headache diagnosis is based on three major sources: 1) criterion variance; 2) information variance; 3) interpretation variance (21) (22) (16). Criterion variance refers to variability in the diagnostic criteria. Criterion variance can be minimised by making the diagnostic criteria more explicit (7) and by using a semi-structured interview (21). We have used a semi-structured interview, with explicit questions containing all the information needed to assign a diagnosis and the physician was free to ask follow-up questions to obtain adequate information. As there is variation in the patient's response to questions (information variance), there is variability in the physician's interpretation of what the patient reports (interpretation variance). Information as well as interpretation variances may always occur despite the application of explicit criteria. For example, an important criterion in diagnosing CEH is question 1:

'the headache is always localised on 1 side of the head' (Table 4). The overall kappa value of this question in our study showed a moderate agreement ( $\text{kappa} = 0.46$ ). In other studies, using clinical records or videotaped interviews, the kappa value for unilaterality ranged from 0.65 to 0.78 (8, 9, 18). A consequence of such an 'in vitro' design is that the information variance is minimised in these studies. Unambiguous information may also reduce interpretation variance. These 'in vitro' studies have shown that the diagnostic criteria of the IHS classification are satisfactorily applicable for the diagnosis of primary headaches when criterion, information and interpretation variance is minimised as far as possible. The clinical relevance of higher kappa scores of some items in these 'in vitro' studies can be debated because of a lack of reflection with patient care. The moderate agreement scores in our study may be caused by information variance from the patients and/or interpretation variance by the different physicians. This is a logic consequence of an 'in vivo' study design when more variance factors are involved. As pointed out before we used a setting resembling the daily clinical practice of most physicians in diagnosing and treating patients with headache. Moreover it should be noted that high kappa scores indicate a good interobserver agreement but are not a guarantee for the accuracy of the diagnosis.

Between pairs of observers kappa was ranging from moderate to almost perfect (Table 2). Almost perfect agreement was measured between the expert headache neurologists ( $\text{kappa} = 0.83$ ). An explanation for this almost perfect agreement could be a more strict employment of the criteria. Between the expert anaesthesiologist in (head) pain treatment (5A+) and the expert headache neurologists (1N+, 2N+) a substantial agreement ( $\text{kappa} = 0.74/0.73$  respectively) was reached. The other kappa values ranged between 0.43 – 0.62 among the other observers indicating a moderate to substantial agreement. In comparison with other studies some of these kappa values are not as high (8, 9, 18). However, in these latter studies all physicians were expert headache neurologists and the study design was an 'in vitro' experiment.

To assess interobserver agreement e.g. on the types of headache, the measurement of kappa is the most adequate method (17). A method to assess whether CEH can be reliably distinguished from migraine without aura and tension-type headache, is the use of a frequency distribution table of the several headache diagnoses (Table 3). Our frequency distribution table shows that CEH is as reliably diagnosable as migraine and even better than tension-type headache.

Diagnostic criteria for CEH differ from the IHS criteria since they include variables obtained by physical examination of the head and the cervical spine (6, 7). We also included these in our study. Physical examination of the cervical spine and occiput revealed only fair group kappa scores concerning the range of motion, moderate kappa scores for pain

provocation with movement and only slight to fair kappa scores regarding pressure pain (Table 5). Strender et al. showed that the kappa score for zygapophyseal joint pressure pain was 0.37 (23). Reliability of different aspects for examining the cervical spine have been investigated in several studies (24-26). These studies have come to various conclusions, most of which suggest low reliability. Other interobserver studies concerning physical examination of the musculoskeletal system confirm these poor reliability results (27-30). Good clinical tests in other medical disciplines operate in the range of 0.4 - 0.6. This, at least, should be the target range for tests in musculoskeletal pain (31). An explanation for the low kappa scores in our study may be the lack of a standardised protocol for physical examination of the musculoskeletal system i.e. the cervical spine. In our study we used no standard protocol on how to perform a physical cervical spine examination because we had the intention to assess the results for each physician who used this examination in daily patient care. Our data show that it is important to agree on how to perform a standard physical examination of the cervical spine and on how to interpret the results.

Our study shows that the reliability in diagnosing CEH, when strictly applying the criteria from Sjaastad et al. (6) is similar to the reliability in diagnosing migraine and tension-type headache according the IHS criteria (7).

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1. *How many people are there in your family?*  
2. *What do you do for a living?*



## CHAPTER 4

### **Interobserver reliability in physical examination of the cervical spine in headache patients**

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## ABSTRACT

The diagnostic criteria for cervicogenic headache include essential items involving the physical examination of the cervical spine. The aim of our study was the assessment of inter-observer reliability between two expert headache neurologists when examining the cervical spine of headache patients.

Twenty-four patients diagnosed as migraine, tension-type headache or cervicogenic headache were included in the study. After an interview each patient's cervical spine was examined in a structured way. Reliability was assessed by Cohen's kappa.

Reduced range of motion in the cervical spine showed kappa values indicating moderate agreement. Provocation of headache revealed a moderate to substantial agreement. Zygapophyseal joint pressure pain assessment showed slight to fair agreement. The kappa values of the circumscribed characteristic tender points showed agreement ranging from 'not better than chance' to 'substantial agreement'.

Our study showed that the interobserver reliability between expert headache neurologists was satisfactory in the majority of the physical examination tests of the cervical spine in patients with different headache syndromes. However, standardisation of the clinical tests, in order to enhance the reliability of these tests is recommended.

**Keywords:** cervical spine, headache, interobserver reliability, kappa, physical examination

Cervicogenic headache (CEH) is a clinically defined headache syndrome which is supposed to originate from nociceptive structures in the cervical or occipital area (1-4). Controversy remains regarding the cervical spine's role in headache (5, 6).

In 1983 Sjaastad and colleagues described the first patients with CEH (1). In 1990 Sjaastad et al. introduced diagnostic criteria for CEH with refinements published in 1998 (7, 8). The main diagnostic problem in CEH patients is to distinguish this headache syndrome from tension-type headache and migraine without aura (9-11). The International Headache Society (IHS) defines criteria for migraine and tension-type headache that include no physical examination tests to diagnose tension-type headache and migraine because they are not relevant to the diagnosis of these headache syndromes (12). In contrast, the criteria for CEH include specific items pertaining to the physical examination of the cervical spine, which are needed to distinguish it from migraine and tension-type headache (8).

An important step in establishing the accuracy of a diagnostic test, such as cervical spine examination, is the investigation of its reliability. Assessment of cervical spine examination has received little attention in the literature despite the high prevalence of neck pain (13, 14). In the absence of a 'reference standard' for the physical examination of the cervical spine, it is imperative that acceptable levels of agreement must be demonstrated for the detection of a given disability in order to establish its diagnostic relevance.

Healthy volunteers and patients with nonspecific chronic neck pain have been subjected to reliability studies of diagnostic tests in the physical examination of the cervical spine. These studies were mainly performed by practitioners of other medical disciplines, such as chiropractors and physiotherapists (15-20). All these studies demonstrated a very wide range of kappa values between 0.00 and 0.80, indicating a poor-to-good reliability. Because there was a lot of variability in the investigated clinical tests in the cervical spine, comparison between the studies was not possible.

To our knowledge, none of these reliability studies have been conducted in patients with CEH. The objective of our study was the assessment of interobserver reliability of two expert headache neurologists in the physical examination of the cervical spine in patients with headache.

Twenty-four patients, 13 males and 11 females, whose mean age was 43 years (range 29 to 59) were included in the study. Patients formerly diagnosed as having CEH, migraine without aura or tension-type headache were included in the study. All subjects were informed of the study and agreed to participate. Patients with CEH, who had been referred by neurologists to the Pain Management and Research Center, were consecutively selected. Patients diagnosed as migraine without aura or tension-type headache according to the IHS criteria were selected at random from the computerised database pertaining to patients with headache from the department of Neurology of the University Hospital of Maastricht. We aimed to have two patients with CEH, two patients diagnosed as migraine without aura and two patients with tension-type headache attend each session. Blinding procedures were guaranteed.

The study was set up in four sessions (I to IV) with six patients and two expert headache neurologists at each session. The two physicians took the history of each patient using a semi-structured interview. After this interview, each neurologist performed a physical examination of the cervical spine in a structured way. Data obtained from these interviews were reported elsewhere (21). The neurologists did not receive any formal instruction in the performance of the physical examination and the amount of pressure applied by each neurologist during palpation was not standardised because we aimed to assess the results for each neurologist who used this examination in daily patient care when indicated. Physical examination of the cervical spine included items that belong to the diagnostic criteria for CEH: 1) functional examination of the cervical spine measuring a reduced range of motion (Table 1, p. 92); 2) provocation of the (head)pain during active movement; and 3) elicitation of a similar (head)pain by external pressure over the ipsilateral upper, posterior neck region or occipital region (Figure 1, p. 94). In order to evaluate the results obtained by pressure in the upper neck and occipital region, we structured this last item in relation to anatomical structures such as the zygapophyseal joints and characteristic points indicating involvement of a segmental level (Table 2). Each examination item was coded (yes/no), and the neurologist assessed whether an impairment was present or not. Abnormal tenderness at the zygapophyseal joints was classified in high-, mid- and low cervical zygapophyseal joint pain. Assessment of abnormal tenderness was always performed on both sides in the cervical spine. The time interval between the physical examinations was less than 25 minutes, and the patients were examined in a random order.

**Table 2. Tenderness at characteristic points in relation to the segmental level.**

Involved segmental level	Characteristic tender points
C <sub>2</sub>	Greater Occipital Nerve (GON)
C <sub>3</sub>	Minor Occipital Nerve (MON)
C <sub>4</sub>	Point just anterior to the trapezius border
C <sub>5</sub>	Point over the trapezius border
C <sub>6</sub>	Point just posterior to the trapezius border
C <sub>7</sub>	Point approximately 3-4 cm. posterior to the trapezius border

Reliability is a measure of agreement between observers and refers to the reproducibility of measurement results or precision of measurements (22, 23). We assessed the interobserver reliability of cervical spine physical examination items. Kappa statistics were used as a measure of interobserver reliability for each item. Kappa adjusts the observed agreement for chance agreement (24). Kappa values were classified as indicating a 'slight', 'fair', 'moderate', 'substantial' and 'almost perfect agreement' according to Landis and Koch (Table 3)(25).

**Table 3. Interpretation the Kappa ( $\kappa$ ) values (25)**

$\kappa < 0$	Less than chance agreement
$\kappa = 0$	Chance agreement
$\kappa = 0.00 - 0.20$	Slight agreement
$\kappa = 0.21 - 0.40$	Fair agreement
$\kappa = 0.41 - 0.60$	Moderate agreement
$\kappa = 0.61 - 0.80$	Substantial agreement
$\kappa = 0.81 - 1.00$	Almost perfect agreement
$\kappa = 1.00$	Perfect agreement

## RESULTS

Assessment of reduced range of motion in the cervical spine for left- and right rotation showed kappa values of 0.44 and 0.46, indicating moderate agreement (Table 1, p. 92). The other movements showed fair agreement values. Assessment of (head) pain provocation with cervical spine movement varied between 0.53 and 0.67, which implies a moderate-to-substantial agreement. Assessment of zygapophyseal joint pressure pain revealed kappa values ranging between 0.14 and 0.37, which indicates slight-to-fair agreement. The mid- and low cervical zygapophyseal

**Table 1. Kappa values per item for physical examination of the cervical spine.**

Items	Kappa value	95% CI
1. Restricted range of motion: flexion	0.27	(-0.17 - 0.70)
2. Restricted range of motion: extension	0.28	(-0.01 - 0.57)
3. Restricted range of motion: rotation right	0.44	(0.10 - 0.79)
4. Restricted range of motion: rotation left	0.46	(0.01 - 0.90)
5. Head pain provocation flexion	0.53	(0.17 - 0.89)
6. Head pain provocation extension	0.67	(0.34 - 0.99)
7. Head pain provocation rotation right	0.65	(0.31 - 0.99)
8. Head pain provocation rotation left	0.54	(0.10 - 0.79)
9. High (upper) zygapophyseal joint pressure pain	0.14	(-0.12 - 0.39)
10. Mid zygapophyseal joint pressure pain	0.37	(0.12 - 0.85)
11. Low zygapophyseal joint pressure pain	0.31	(0.28 - 0.90)
12. Pressure pain occiput right (GON) <sup>1</sup>	0.00	(-1.00 - 0.77)
13. Pressure pain occiput left (GON) <sup>1</sup>	0.16	(-0.31 - 0.61)
14. Pressure pain mastoid process right	0.77	(0.34 - 1.00)
15. Pressure pain mastoid process left	1.00	
16. Pressure pain insertion m.SCM <sup>2</sup> on occiput right (MON) <sup>3</sup>	0.68	(0.29 - 1.00)
17. Pressure pain insertion m.SCM <sup>2</sup> on occiput left (MON) <sup>3</sup>	0.35	(-0.17 - 0.86)
18. Pressure pain just anterior to the m.SCM <sup>2</sup> border right	0.35	(-0.17 - 0.86)
19. Pressure pain just anterior to the m.SCM <sup>2</sup> border left	0.55	(0.10 - 0.99)
20. Pressure pain over the m.SCM <sup>2</sup> border right	0.52	(0.12 - 0.92)
21. Pressure pain over the m.SCM <sup>2</sup> border left	0.42	(0.01 - 0.82)
22. Pressure pain just posterior to the m.SCM <sup>2</sup> border right	0.60	(0.19 - 1.00)
23. Pressure pain just posterior to the m.SCM <sup>2</sup> border left	0.87	(0.62 - 1.00)
24. Pressure pain 3-4 cm posterior to the m. SCM <sup>2</sup> border right	0.68	(0.28 - 1.00)
25. Pressure pain 3-4 cm posterior to the m.SCM <sup>2</sup> border left	0.77	(0.34 - 1.00)

<sup>1</sup> GON = Greater Occipital Nerve

<sup>2</sup> m.SCM = musculus sternocleidomastoideus

<sup>3</sup> MON = Minor Occipital Nerve

joints were more 'reliable' when investigated than the higher joints. The kappa values of the circumscribed characteristic tender points ranged between 0.00 and 1.00. Pressure pain on the occiput demonstrated an agreement no better than chance. Tender points with substantial agreement were pressure pain on the mastoid process and pressure pain posterior to the sternocleidomastoid muscle border on both sides. The other tender points showed fair-to-moderate agreement.

## DISCUSSION

Physical examination of the cervical spine is a crucial part of the diagnosis CEH. In our study, we found that interobserver reliability regarding the physical examination of the cervical spine for patients with different types of headache, for two expert headache neurologists, is acceptable for the majority of the items. Bogduk concludes that for most good clinical tests in physical examination the kappa value should range between 0.4 and 0.6 (26). Although different cut-off points for kappa values are used for defining poor-to-perfect reliability, there is consensus that the minimum value of acceptable agreement by any set of guidelines is a kappa value of 0.4 (27-30). We used the arbitrary scale of Landis and Koch, in which kappa values ranging from 0.4 to 0.6 suggest moderate agreement (25).

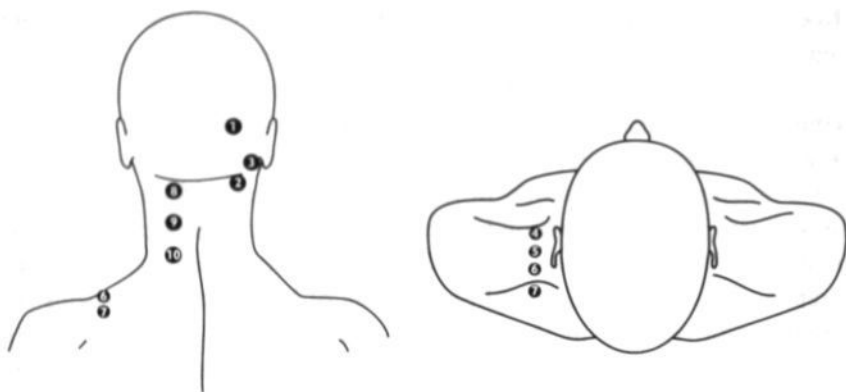
Our results showed that assessment of (head) pain provocation could be reliably diagnosed. This is in accordance with another reliability study that assessed pain provocation (18).

Impairment of rotation in the cervical spine could be reliably assessed using visual estimation in our study. Restriction of flexion and extension could not be assessed reliably. A possible explanation for this discrepancy in kappa values might be the use of left/right comparisons for rotation movements in the assessment of restriction. Hendriks et al. showed a substantial agreement score in one practice and slight agreement score in the other practice (18). In their study, no differentiation was made in the assessment between patients with low back pain and those with neck-shoulder pain. Hendriks et al. only diagnosed a decrease in range of motion without any differentiation in motion direction. It is known that the more choice a clinician has in grading a single observation, such as a decreased range of motion, the greater the resulting interobserver error will be (31, 32).

It has been suggested that CEH could originate from dysfunction of the cervical zygapophyseal joints (3, 19, 33, 34). Physical examination of the cervical spine in order to reveal zygapophyseal joint pressure pain, possibly indicating involvement of these joints in the CEH syndrome, demonstrated only fair agreement. This is in accordance with the results of Strender et al. who showed only fair agreement (20). Strender et al. used volunteers in their study. It could be argued that it is difficult to obtain clinically relevant conclusions from reliability studies of clinical tests in volunteers. In contrast to the results of Strender et al., Hubka and Phelan showed substantial agreement in their study (17). They studied 30 patients with 'unilateral mechanical neck pain' and they standardised the palpation method. Hubka and Phelan concluded that palpation for zygapophyseal joint pain is a highly reliable tool. Conversely, some authors claim that physical examination at the spine reveals no specific features

that identify whether a cervical zygapophyseal joint is painful or not (35-37). As a consequence, they advocate the use of controlled diagnostic blocks. A disadvantage of diagnostic blocks is that they do not identify the pain source; they only imply that the pain is transmitted by that nerve (38). Jull et al. compared the diagnostic accuracy of manual palpation with that of diagnostic nerve blocks (39). They found that assessment of palpation could identify the presence and location of the painful zygapophyseal joints with 100% sensitivity and specificity compared with diagnostic nerve blocks.

Figure 1.



Points at which pressure pain on palpation was assessed:

- 1 = occiput (GON<sup>1</sup>)
- 2 = insertion of m.SCM<sup>2</sup> at occiput (MON<sup>3</sup>)
- 3 = mastoid process
- 4 = immediately anterior to the m.SCM<sup>2</sup> border
- 5 = border of m.SCM<sup>2</sup>
- 6 = just posterior to the m.SCM<sup>2</sup> border
- 7 = a point 3 to 4 cm. posterior to the m.SCM<sup>2</sup> border
- 8 = high zygapophyseal joint level
- 9 = mid zygapophyseal joint level
- 10 = low zygapophyseal joint level

<sup>1</sup> GON = Greater Occipital Nerve

<sup>2</sup> m.SCM = *musculus sternocleidomastoideus*

<sup>3</sup> MON = Minor Occipital Nerve

Some authors suggest that circumscribed abnormal tenderness at characteristic points on physical examination may have a frequent, but inconsistent, relationship with segmental levels (Figure 1)(40). Assessment of the characteristic tender points demonstrated variable reliability scores ranging from agreement that was no better than chance to perfect agreement. However, the results in Table 1 show that only pressure pain on the occiput was not reliable. The other characteristic tender points demonstrated, in general, agreement that was moderate to almost perfect. Strender et al. showed a kappa value of 0.31 for trapezius muscle pain. The relationship of positive circumscribed tender points with any form of treatment or radiological confirmation of a pathological 'focus' is still not established. It must be emphasised that our study was only designed to test the agreement between positive or negative results. Furthermore, it is important to realise that kappa is a measure of agreement between two observers, but it is never a guarantee of the accuracy of the result.

Our study showed that the interobserver reliability of two expert headache neurologists was satisfactory in the majority of the physical tests used in the examination of the cervical spine in patients with different headache syndromes. However, it is highly questionable whether such satisfactory results would be obtained by physicians not experienced at diagnosing headache syndromes. Clearly, since both the IHS and CEH diagnostic classifications include items obtained from the physical examination of the cervical spine, more explicit guidelines should be developed to increase standardisation of headache diagnosis.

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$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \left( \frac{1}{2} \frac{d}{dt} \right) \\ & \frac{1}{2} \frac{d}{dt} \left( \frac{1}{2} \frac{d}{dt} \right) \\ & \frac{1}{2} \frac{d}{dt} \left( \frac{1}{2} \frac{d}{dt} \right) \end{aligned}$$

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## CHAPTER 5

### **Quality of life in cervicogenic headache – a comparison with healthy subjects, migraine and tension-type headache patients**

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Submitted

## ABSTRACT

**Objective:** The purpose of this study was to establish the health related quality of life (HRQoL) of patients with cervicogenic headache (CEH) and to compare it with a random Dutch sample of healthy persons (reference group), and with patients with migraine without aura or episodic tension-type headache.

**Methods:** Thirty-seven CEH patients, forty-two patients with episodic tension-type headache and thirty nine patients with migraine without aura completed a Medical Outcomes Study Short Form-36 (MOS SF-36) questionnaire.

**Results:** All MOS SF-36 domain scores were significantly lower for patients with CEH relative to the healthy reference group. Comparison of the domain scores between CEH and migraine showed that 'physical functioning' (PF) was significantly more affected in CEH. Comparison between CEH and tension-type headache revealed a worse score for 'physical functioning' (PF) for CEH. The domain 'physical functioning' (PF) scored lower for tension-type headache than for migraine. Migraineurs reported a diminished score for 'social functioning' (SF) compared to tension-type headache patients.

**Conclusion:** Patients with CEH have a quality of life burden that is substantial. Although the impairment in quality of life in CEH is comparable with migraine without aura and episodic tension-type headache, there are some specific differences compared with migraine without aura and episodic tension-type headache.

**Keywords:** cervicogenic headache, mental health status, quality of life, SF-36 questionnaire

## INTRODUCTION

Cervicogenic headache (CEH) is a clinically defined headache syndrome hypothesised to originate from nociceptive structures in the cervical or occipital area (1-4). Although the diagnosis of CEH is controversial (5, 6) (it is not included in the IHS classification), we have recently demonstrated the clinical validity to diagnose this headache syndrome (7, 8). There is increasing literature on the diagnosis and treatment of CEH, but epidemiological data are scarce (9). In particular, little is known about the extent to which the quality of life is impaired in CEH.

Many studies underscore the impact of chronic headaches on patients' quality of life (10-16). Although there is some debate on how quality of life should be measured in headache patients, consensus exists that health-related quality of life (HRQoL) is a reliable tool to assess quality of life (10, 12, 16, 17). HRQoL is an expression of individuals' perceptions of their position in life that is affected by their physical health, psychological state and social relationships. HRQoL includes subjective perceptions of one's life situation in the context of the culture and value system in which they live and in relation to their goals, expectations and standards.

Assessment of HRQoL makes it possible to quantify the burden of illness and to compare the burden with healthy people or among different disorders e.g. headaches. The subjective nature of headache and the absence of objective clinical end points have left clinicians without an objective standard by which to judge the impact of headache on patients. Therefore instruments measuring the HRQoL have been developed to assess functional status and well-being of the headache patient. The RAND Corporation has developed such an instrument of HRQoL assessment. The Medical Outcomes Study (MOS) Short Form (SF-36) questionnaire has been used to address this issue (15, 18, 19). The SF-36 is a brief generic questionnaire and also serves as a valuable instrument determining differences in functional status and well-being among the different headache syndromes (12).

Up till now, all reports refer to HRQoL studies in migraine, tension-type headache, chronic daily headache or cluster headache patients. There is no previous experience in assessing the HRQoL in patients with CEH. The aim of our study was to apply the SF-36 questionnaire to patients with CEH and to determine the impact on HRQoL in these patients, and to evaluate differences in functional health status between CEH, migraine without aura and episodic tension-type headache.

## PATIENTS AND METHODS

The Medical Ethical Committee of the University Hospital Maastricht approved the study protocol, and written informed consent from every patient was obtained before entry into the study. The study sample consisted of one hundred and eighteen headache patients, 80 females and 31 males (Table 1).

**Table 1.** Demographic information about cervicogenic headache, episodic tension-type headache and migraine without aura.

Headache	N	Gender		Age	
		Male	Female	Mean	SD
CEH	37	10 (27.0%)	27 (73.0%)	48.3	11.1
TTH	42	14 (33.3%)	28 (66.7%)	41.4	14.5
Migraine	39	9 (23.1%)	30 (76.9%)	39.1	11.1

*CEH = cervicogenic headache*

*TTH = episodic tension-type headache*

*SD = Standard Deviation*

Only those diagnosed as having migraine without aura, episodic tension-type headache or CEH were included in the study. Experienced neurologists made the various headache diagnoses. Patients with migraine without aura or episodic tension-type headache were diagnosed according to the IHS classification (20). Patients with CEH were diagnosed according to the criteria from Sjaastad et al. (21). Patients were recruited in two ways: 1) during their first appointment with their neurologist or 2) at random from the computerised headache patient database from the Department of Neurology of the University Hospital Maastricht. During the initial visit and after completing the inclusion and exclusion criteria list (Table 2), patients were asked by their physician to participate in the study. Other (chronic) illnesses that might confound the HRQoL, such as diabetes mellitus, chronic musculoskeletal pain syndrome, depression etc., were listed in the exclusion criteria list. Treatment was started after completing the SF-36 questionnaire. Patients selected from the computerised list were questioned using a semistructured interview by telephone by an experienced clinician (JvS) to verify whether their original headache, i.e. migraine without aura or episodic tension-type headache, was unchanged at present in spite of treatment. The presence of comorbid conditions as well as other exclusion criteria (Table 2) was checked during the semistructured interview. The patients who fulfilled the inclusion criteria were

asked to participate in the study. An appointment was made within a few days at the Pain Management and Research Centre of the University Hospital Maastricht. All patients filled out their questionnaire at the hospital. The data manager (SS-vdB or IL) checked the questionnaires for missing data before the patient left the hospital.

**Table 2. Inclusion – and exclusion criteria**

**Inclusion criteria:**

1. Patients fulfilling the IHS criteria for migraine without aura or episodic tension-type headache.
2. Patients with cervicogenic headache fulfilling the criteria according to Sjaastad et al.
3. Headache diagnosis were made by experienced neurologists.
4. Age between 18-65 years.
5. Headache duration at least 6 months.
6. Headache syndrome without positive treatment results.
7. Informed consent.

**Exclusion criteria:**

1. Other illnesses that might confound the association between headache and the quality of life such as:
  - diabetes mellitus
  - chronic musculoskeletal pain syndrome
  - other chronic (pain) syndromes
2. Patients with psychiatric disorders such as depression etc.
3. Patients without any headache complaints as a result of treatment.
4. Patients with more than one headache syndrome.

The questionnaire used for measuring HRQoL was the Dutch version of the SF-36. The translated Dutch version of the SF-36 is a practical, reliable and valid questionnaire for use among the Dutch speaking population of The Netherlands (22, 23). The most widely used generic questionnaire to assess HRQoL for primary headache syndromes is the SF-36 (10, 12, 13, 15, 16, 23-25). The SF-36 questionnaire exhibited the best ability to discriminate between healthy controls and subjects who suffer from health problems (26-28). The SF-36 measures physical, functional, mental and social health. The SF-36 consists of 36 items representing eight generic health domains: 1) physical functioning (PF); 2) social functioning (SF); 3) role limitations physical (RP); 4) role limitations emotional (RE); 5) mental health (MH); 6) vitality (VT); 7) bodily pain (BP); 8) general health perceptions (GH). Definitions of each domain are listed



in Table 3. The SF-36 domain scores were taken from the SF-36 Health Survey Manual and Interpretation Guide (29). The raw item scores of the SF-36 questionnaire were summed up to form domain scores and transformed to a 100-point scale. The SF-36 domain scores range between 0 to 100, a high score indicates a higher level of functioning or well-being.

**Table 3. Domains of the SF-36**

Domain	No. Items	Definition
Physical functioning	10	Capacity to perform a variety of common physical activities
Social functioning	2	Extent to which health interferes with normal social activities
Role limitations physical	4	Degree to which physical health interferes with usual daily activities
Role limitations emotional	3	Extent to which emotional problems interfere with usual daily activities
Mental health	5	General mood or affect in past 4 weeks
Vitality	4	General energy, level of fatigue in past 4 weeks
Bodily pain	2	Pain during past 4 weeks
General health perceptions	5	Overall assessment of health in general

We analysed the domain scores of the CEH group and compared them with a healthy reference group. The reference group domain scores were derived from a study by Van der Zee et al. (22). This reference group (N = 295) was chosen from a random sample survey from the population register of Emmen, a Dutch city in The Netherlands. The mean age of this group was 44.1 years, ranging from 18 to 89 years and with a female preponderance of 65%. Because three domain scores (i.e. 'physical functioning' (PF), 'role physical' (RP) and 'role emotional' (RE) were not normally distributed, we analysed our data using the Mann-Whitney non-parametric test. However, to compare our results with those of other studies, which used Student-t tests, we also performed this analysis comparing the HRQoL of CEH with that of migraine and tension-type headache. No substantial differences were found in the analysis of our results with the parametric Student-t test. In this study, the scores of the eight SF-36 domains were compared among the three headache diagnoses by one-way analysis of variance (ANOVA). Statistical significance was set at  $P < 0.05$ . We used the statistical software package for social sciences (SPSS 9.0).

## RESULTS

One hundred eighteen patients (Table 1) completed the SF-36 questionnaire. The mean ages in the different groups, i.e. CEH, tension-type headache and migraine, were 48.3 years (SD 11.1), 41.4 years (SD 14.5) and 39.1 years (SD 11.1) respectively. There was a statistical difference ( $P < 0.05$ ) in the mean age between CEH and migraine and between CEH and tension-type headache. Patients with CEH were older. Between migraine and tension-type headache no significant difference in mean age was found. In all groups there was a female preponderance in 73.0%, 66.7% and 76.9% of patients with CEH, tension-type headache and migraine, respectively. The reference group was not significantly different from the CEH group with respect to age and gender. Missing SF-36 data were not detected.

The SF-36 mean domain scores of the CEH group were all significantly worse than those of the reference group (Table 4). The HRQoL of patients suffering from CEH was most profoundly affected in the domains 'role physical' (RP) and 'bodily pain' (BP) (Figure 1).

**Table 4.** Comparison of mean health-scale scores between cervicogenic headache patients (n=37) and the reference-group (n=292).

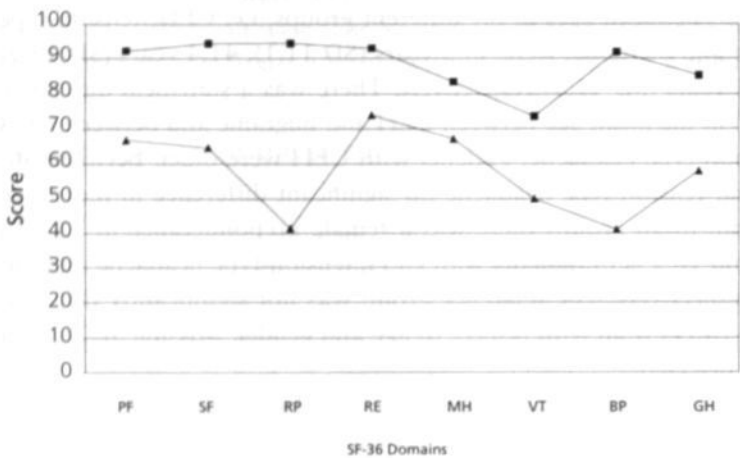
Scale	Group	Mean score	SD	p-value	95% CI
Physical function (PF)	CEH	66.8	23.1	$< 0.001$	$25.4 \pm 19.9$
	Reference	92.2	13.0		
Social function (SF)	CEH	64.5	23.7	$< 0.001$	$29.7 \pm 22.3$
	Reference	94.2	12.3		
Role physical (RP)	CEH	41.2	38.3	$< 0.001$	$53.1 \pm 37.0$
	Reference	94.3	19.4		
Role emotional (RE)	CEH	73.9	35.3	$< 0.001$	$19.2 \pm 26.8$
	Reference	93.1	21.6		
Mental health (MH)	CEH	67.1	17.8	$< 0.001$	$16.2 \pm 8.8$
	Reference	83.3	13.3		
Vitality (VT)	CEH	50.0	18.6	$< 0.001$	$23.4 \pm 10.1$
	Reference	73.4	13.5		
Bodily pain (BP)	CEH	40.9	22.3	$< 0.001$	$50.9 \pm 12.1$
	Reference	91.8	16.1		
General health (GH)	CEH	58.1	18.9	$< 0.001$	$27.0 \pm 11.6$
	Reference	85.1	13.0		

CEH = cervicogenic headache

SD = Standard Deviation

95% CI = 95% confidence interval

Figure 1: Mean health scale scores in CEH (▲), and in the reference-group (■).



All values are statistical significant  $P < 0.001$

ANOVA statistics showed a level of significance only for ‘physical functioning’ (PF). Comparison of the SF-36 mean domain scores between CEH, migraine and tension-type headache are given in Table 5.

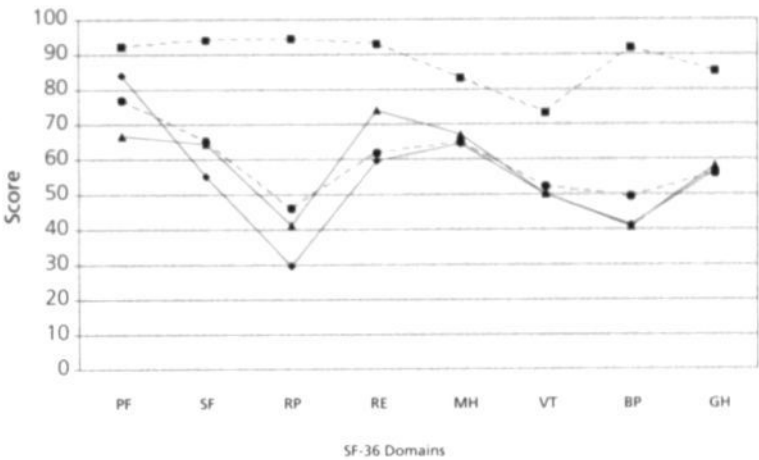
Table 5: Comparison of mean health-scale and standard deviationscores between patients with cervicogenid headache, migraine without aura or episodic tension-type headache.

	Physical function (PF)	Social function (SF)	Role phys (RP)
CEH	66.8 (23.1)	64.5 (23.7)	41.2 (38.5)
Migraine	83.9 (20.5)	55.1 (21.4)	29.5 (33.5)
p-value	0.001	ns	ns
CEH	66.8 (23.1)	64.5 (23.7)	41.2 (38.5)
TTH	77.0 (20.7)	65.2 (22.0)	45.8 (42.5)
p-value	0.03	ns	ns
Migraine	83.9 (20.5)	55.1 (21.4)	29.5 (33.5)
TTH	77.0 (20.7)	65.2 (22.0)	45.8 (42.5)
p-value	0.05	ns	ns

Significance  $P < 0.05$ ; ns = not significant

The mean domain score for ‘physical functioning’ (PF) was significantly worse for CEH compared with migraine and tension-type headache. Compared with migraineurs, tension-type headache patients scored lower on the dimension ‘physical functioning’ (PF). Figure 2 shows the scores for healthy subjects and patients with CEH, migraine and tension-type headache as outlined in Table 5.

Figure 2: Mean health-scale scores in CEH (▲), TTH (●), migraine (◆) and in the reference-group (■).



Role emotional (RE)	Mental health (MH)	Vitality (VT)	Bodily pain (BP)	General health (GH)
73.9 (35.3)	67.1 (17.8)	50.0 (18.6)	40.9 (22.3)	58.1 (18.9)
59.8 (45.4)	64.4 (21.0)	50.0 (16.9)	41.1 (19.1)	56.5 (21.5)
ns	ns	ns	ns	ns
73.9 (35.3)	67.1 (17.8)	50.0 (18.6)	40.9 (22.3)	58.1 (18.9)
61.9 (43.3)	64.7 (17.8)	52.4 (17.2)	49.3 (20.7)	56.1 (22.1)
ns	ns	ns	ns	ns
59.8 (45.4)	64.4 (21.0)	50.0 (16.9)	41.1 (19.1)	56.5 (21.5)
61.9 (43.3)	64.7 (17.8)	52.4 (17.2)	49.3 (20.7)	56.1 (22.1)
ns	ns	ns	ns	ns

## DISCUSSION

Patients with CEH have never been subjected to assessment of HRQoL. This is the first study demonstrating that patients with CEH have worse HRQoL than a healthy community sample (Table 4). They score significantly worse on all eight SF-36 domains indicating that in CEH the degree of disability is substantial and must not be underestimated (Fig. 1). The lowest domain scores (i.e. < 50) in CEH patients were found in 'role physical' (RP) and 'bodily pain' (BP). Patients with migraine or tension-type headache in our study also had the lowest domain scores in 'role physical' (RP) and 'bodily pain' (BP). These results are consistent with the findings in other headache studies although the level of severity differs e.g. 'bodily pain' (BP) scores are worse in cluster headache compared to CEH, migraine or tension-type headache (10, 12, 16).

As quality of life is affected in headache, we sought to assess this in CEH. Solomon et al. found, using the SF-20 questionnaire, that distinct headache diagnoses, such as migraine, tension-type headache and cluster headache according to the IHS criteria, are marked by unique patterns of impairment in quality of life (13). Because we have shown that CEH is a distinct headache syndrome (7), the question arises whether the pattern of HRQoL in CEH is unique. Comparison between the patterns in the study from Solomon et al. with our CEH patients is not possible because he used the SF-20 questionnaire which is the precursor of the SF-36 questionnaire. We found that the domain score for 'physical functioning' (PF) differed significantly between CEH and migraine in our study (Table 5). A worse score for 'physical functioning' (PF) means that common daily activities such as walking, shopping, cleaning the house etc. are impaired. It has been shown that the impact of headache on HRQoL in patients depends to a great extent on the chronicity of the headache (16) or the frequency of attacks (30). Although the pattern of headache attacks may vary intra-individually in CEH patients, eventually it develops into a more or less chronic fluctuating pattern in most patients (1, 4). Therefore, more days with a headache could be an explanation for the lower score for 'physical functioning' (PF) in our CEH patients. However, in our study we have not adjusted our data for the frequency of migraine attacks nor for the days with headache in CEH or tension-type headache.

Comparing the domain scores in migraine patients from Monzón's study with our CEH patients demonstrates that 'physical functioning' (PF) is the only significantly different domain score (Table 6). We also compared our data with the results from population-based quality of life studies in migraine patients, which used the SF-36 questionnaire (Table 6) (12, 23). We found that 'physical functioning' (PF) was also statistically significant worse in patients with CEH compared with migraineurs from these studies. Furthermore, whether this is a unique pattern of impairment

for CEH or just a coincident finding related to the more chronic character of the headache and/or older age group of CEH remains to be established.

**Table 6.** Comparison of mean health-scale scores and standard deviation between patients with cervicogenic headache and migraine in several migraine studies.

	CEH (Van Suijlekom) (n= 37)	Migraine (Van Suijlekom) (n= 39)	Migraine (Monzón) (n= 62)	Migraine (Osterhaus) (n= 546)	Migraine (Aaronson) (n= 400)
<b>Domains</b>					
PF	66.8 (23.1)	83.9 (20.5)***	83.8 (18.1)**	83.2 (18.7)**	81.4 (21.1)**
SF	64.5 (23.7)	55.1 (21.4)	71.6 (23.2)	71.1 (23.3)	73.1 (20.4)
RP	41.2 (38.3)	29.5 (33.9)	49.2 (41.8)	54.0 (44.4)	54.6 (40.4)
RE	73.9 (35.3)	59.8 (45.4)	71.5 (37.1)	66.5 (44.4)	73.3 (37.6)
MH	67.1 (17.8)	64.4 (21.0)	64.0 (18.6)	66.4 (18.7)	70.1 (19.1)
VT	50.0 (18.6)	50.0 (16.9)	54.4 (22.4)	50.9 (21.0)	58.9 (19.7)*
BP	40.9 (22.3)	41.1 (19.1)	46.3 (20.9)	51.3 (23.4)*	58.6 (21.4)***
GH	58.1 (18.9)	56.5 (21.5)	62.5(18.8)	70.1 (21.0)*	64.7 (20.0)

\*  $P < 0.05$

\*\*  $P < 0.001$

\*\*\*  $P < 0.0001$

The SF-36 domain 'bodily pain' (BP) measures the severity of the pain i.e. the headache, as well as to which extent the pain affects normal daily activities during the last 4 weeks. Patients with CEH demonstrated a substantially worse score for 'bodily pain' (BP) compared with the reference group (Table 4). Although CEH patients demonstrated the lowest score in 'bodily pain' (BP), it differed not significantly with the 'bodily pain' in patients with migraine or tension-type headache in our study (Table 5). However, comparing our results regarding 'bodily pain' (BP) with other studies, we found a statistically significant difference with the studies from Osterhaus and Aaronson but not in Monzón's study (Table 6) (12, 16, 23). A possible explanation for this significant difference in 'bodily pain' (BP) could be the method of patient selection. Patients in our study and from Monzón's were recruited from hospitals while the patients from Aaronson et al. and from Osterhaus et al. were selected from the community. On average, patients with headache who consult physicians and specialised headache clinics have more severe headache than pa-

tients in the community (10, 13, 31, 32). Some other domain scores in the two population-based migraine studies were also significantly different compared to CEH, however without a consistent pattern (Table 6). It must be stressed that comparison of data from the SF-36 questionnaires between studies should be done cautiously due to confounding factors such as patient selection, cross-cultural differences etc.

The present data demonstrate that the impairment in quality of life in CEH is worse compared to healthy persons but is, in general, comparable with migraine and tension-type headache. Although there is no previous experience in CEH, our results suggest that the SF-36 questionnaire is valuable in determining differences in quality of life among different headache syndromes and might be used as a primary outcome measure in clinical trials on CEH. CEH may have an unique pattern of disability compared to migraine, where 'physical functioning' (PF) is concerned. However, this may be due to the more chronic character of this headache and therefore not specific for CEH.

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## CHAPTER 6

### Cervicogenic headache: techniques of diagnostic nerve blocks

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## ABSTRACT

The term cervicogenic headache (CEH) was introduced by Sjaastad and coworkers in 1983. In 1990 Sjaastad et al. published diagnostic criteria for CEH. In 1998 refinements of these criteria were published emphasising the use of diagnostic nerve blocks in patients with CEH as an important confirmatory evidence. However, the standardisation of diagnostic nerve blocks in the diagnosis of CEH remains to be defined. Herein we present an overview of diagnostic nerve blocks in the cervical area. Suggestions as to their role in the diagnosis of CEH are given.

**Keywords:** cervicogenic headache, diagnostic nerve block, greater occipital nerve block, intervertebral disc block, minor occipital nerve block, segmental nerve block, zygapophyseal joint block

## INTRODUCTION

Cervicogenic headache (CEH) is a clinically defined headache syndrome which is hypothesised to originate from nociceptive structures in the cervical spine. Early publications of this concept were offered by Barré, Bärtschi-Rochaix and Hunter and Mayfield (1-3). In 1983 Sjaastad and colleagues introduced the term cervicogenic headache (CEH) to describe a headache arising from the neck radiating to ipsilateral frontotemporal and orbital regions (4). CEH is, in principle, a unilateral headache without sideshift but it may also be bilateral. A diffuse, ipsilateral neck, shoulder, or arm pain of a nonradicular nature may occur. Symptoms and signs referable to the cervical spine are essential. In 1990 Sjaastad et al. published the first diagnostic criteria for CEH (5). In these criteria, diagnostic nerve blocks with the use of a local anaesthetic solution were not mandatory. Recently refinements of these criteria were published adding the use of diagnostic nerve blocks as an important confirmatory evidence in diagnosing CEH (6). Moreover, a positive response to a diagnostic nerve block is an obligatory point for CEH in scientific work.

A possible neuro-anatomical basis for CEH is convergence in the trigeminocervical nucleus between nociceptive afferents from the field of the trigeminal nerve and the receptive fields of the first three cervical nerve roots (7-11). This may imply that CEH mainly emanates from structures innervated by the first three cervical nerve roots whereby the C2 cord segment is an important relay of afferent fibres (12, 13). However, other observations suggest that headache may also arise from structures in the lower cervical spine (14-16). Various structures in the cervical spine are capable of causing neck pain and headache such as the zygapophyseal joints, segmental nerves, dorsal root ganglia, intervertebral discs, muscles and ligaments (11, 15, 17-19). Other authors have reported the existence of venous vascular and non vascular compression of the upper cervical roots in patients with CEH (20, 21).

Although diagnostic nerve blocks are an obligatory point in establishing the diagnosis CEH, description of the techniques is absent. The aim of this paper is to summarise existing literature on techniques of diagnostic nerve blocks in the cervical area.

A diagnostic block is a temporary reversible block with a local anaesthetic solution directed to a target nervous structure with the intention to relieve the (head)pain. Not every anatomical structure in the cervical spine which is innervated e.g. dura mater and vertebral artery, can be blocked reliably. This may be due to: 1) problems to approach the anatomical structure safely; 2) a multisegmental innervation of the structure.

Diagnostic blocks should be directed to the nerve(s) or structure(s) suspected of mediating or causing CEH. Appropriate blocks in the cervical spine should include structures capable of causing CEH such as: the greater occipital nerve (GON), minor occipital nerve (MON), zygapophysial joints (facet joints), segmental nerves and intervertebral discs (6, 13, 16). Sometimes additional information may be obtained by combining diagnostic nerve blocks. Diagnostic blocks aimed at deeper anatomical structures should be done using fluoroscopic control to enhance reliability (22-24). It is also recommended to use a contrast medium (Iohexol, Omnipaque 240®) to check the position of the needle at the target and to prevent intravascular or intrathecal injection. The quantity of the local anaesthetic solution should be as small as possible to prevent overflow to other structures. Severe coagulation disturbances are a contra-indication to perform the more invasive diagnostic blocks. Pain relief after diagnostic nerve block is generally assessed 30 minutes after the procedure by means of a 4 point Verbal Rating Scale and a VAS scale.

## TECHNIQUES OF DIAGNOSTIC NERVE BLOCKS

### *Technique of a diagnostic block of the greater occipital nerve*

The greater occipital nerve (GON), the medial branch of the C2 dorsal ramus, is technically easy to perform (18, 25-27). A 22G needle is placed approximately 2 cm. lateral and 2 cm. inferior to the external occipital protuberance. After contact with the periosteum of the occipital bone the needle is withdrawn approximately 0.5 cm. before injection. The injected volume is 1.0-2.0 ml. of a local anaesthetic solution e.g. Lidocaine 2%. Assessment of sensory deficit of the ipsilateral scalp is performed to confirm the accuracy of injection near the GON. Fluoroscopy is not indicated for this peripheral nerve block.

### *Technique of a diagnostic block of the minor occipital nerve*

The minor occipital nerve (MON) arises from the ventral ramus of C2 with a variable contribution of the ventral ramus of C3 (28). The sensory innervation area is behind the ear. A diagnostic block of this nerve is performed with a 22 G needle inserted at the mastoid process posterior to

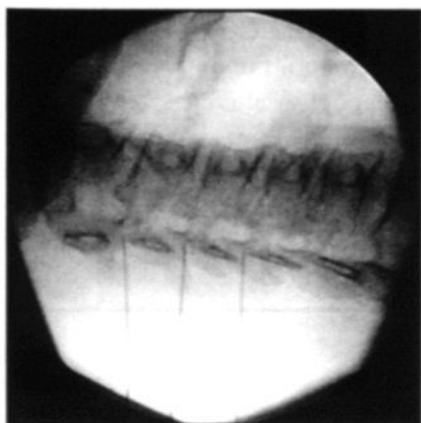
the ear. The injected volume is 1-2 ml Lidocaine 2%. Sensory loss is assessed to control appropriate injection near the MON. Fluoroscopy is not indicated.

### *Technique of a diagnostic block of the zygapophyseal joints*

The zygapophyseal joints are innervated by the medial branches of the dorsal rami of the segmental nerves (29, 30). Each zygapophyseal joint is ipsilaterally and bisegmentally supplied by branches from the dorsal ramus of its own segment and from one level more cephalad. As a consequence, a diagnostic block of one zygapophyseal joint involves a block of two adjacent medial branches of the dorsal rami.

There are two reliable techniques to perform a diagnostic block of the zygapophyseal joints: a) the dorsal-lateral approach (31); b) the lateral approach (32).

In the dorsal-lateral approach, the patient is positioned supine on the operating table. The C-arm of the fluoroscopy equipment is positioned slightly oblique so that the X-ray are parallel to the axis of the intervertebral foramen which is upwards and slightly caudal (24, 31). The dorsal ramus in this projection runs over the base of the superior articular process (Figure1). Entry points of the needles are marked posterior to the posterior border of the bony collumn of the zygapophyseal joints and slightly caudal to the target point. A 22 Gauge 50 mm. Neurography® needle (Radionics) is introduced and carefully advanced anteriorly and cranially untill contact is made with the base of the processus articularis superior. The position of the C-arm is changed to the anterior-posterior (AP) direction. This should confirm the position of the tip of the needle adjacent to the 'waist' of the articular pillars of the cervical spine at the corresponding level (Figure 2). To avoid an intravascular injection 0.2-0.3 ml of contrast medium (Iohexol, Omnipaque 240®) is injected. The injected volume of local anaesthetic solution is 0.5 ml. Lidocaine 2%.



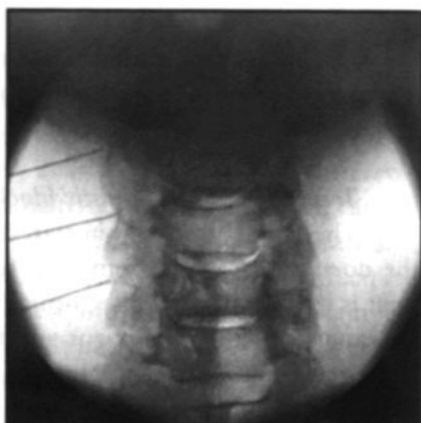
**Figure 1**

Diagnostic nerve block of the medial branches of dorsal the rami C3, C4 and C5. The needles are positioned at the base of the superior articular processes and make contact with bone. C-arm in 20°- 30° oblique and 10° caudocranial projection.



**Figure 2.**

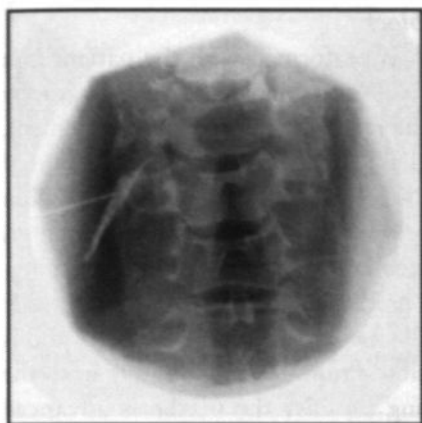
Diagnostic nerve block of the medial branches of dorsal the rami C3, C4 and C5. The needles are positioned in the 'waist' of the articular pillars. C-arm in AP projection.



In the lateral approach, the patient is positioned supine on the operating table. The C-arm of the image intensifier is positioned in a lateral projection. Target point is the centroid of the articular pillar. Entry points are marked over the centroid and 22 G Neurography® needles are advanced in lateral projection until contact is made with bone of the articular pillar (32). After injection of 0.2-0.3 ml. contrast medium, 0.5 ml. of Lidocaine 2% is injected.

### *Technique of a diagnostic segmental nerve block*

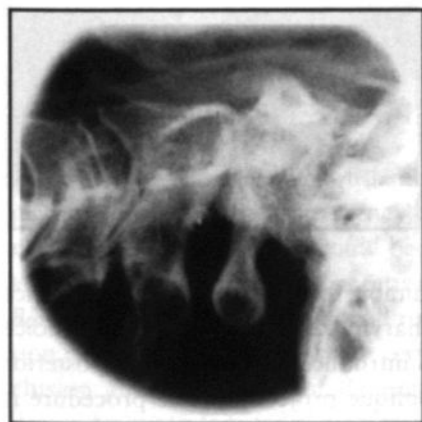
A diagnostic segmental nerve block at the levels C3, C4 and C5 is performed using the C-arm fluoroscopy equipment positioned to have the X-rays parallel to the axis of the intervertebral foramen (23, 24, 31). This axis points 25-35° anteriorly and 100° caudally. With the C-arm in this position, the entry point is found by projecting a metal ruler over the caudal part of the foramen. A 50 mm. 22G Neurography® needle (Radionics) is introduced in the direction of the X-rays. If necessary the direction is corrected while the tip is still in the superficial layers, until the needle is projected on the monitor screen as a dot ('tunnel vision' technique). In practise this dot should lie directly over the dorsal wall of the caudal part of the intervertebral foramen. The direction of the C-arm is then changed to AP and the canula is further introduced until the tip is projected just lateral from the bony column of the zygapophyseal joints. After the segmental nerve has been identified with 0.2-0.3 ml. contrast medium (Iohexol, Omnipaque 240®), 0.5 ml. Lidocaine 2% is slowly injected (Figure 3). During the injection the resultant radio-opaque mixture is observed to avoid accidental overflow into the epidural space. Relief of headache will be assessed 30 minutes after the procedure.



**Figure 3**

Diagnostic segmental nerve block C3. C-arm in AP projection after injection of 0.2-0.3 ml. contrast medium (Iohexol, Omnipaque 240®).

At the level C2 a diagnostic nerve block is performed differently since the anatomy at that level is different. The foramina start at the C3 level. The C2 nerve exits from the arch of the atlas (C1) and the lamina of the axis (C2). The C-arm is positioned in a lateral view and the arch is visualised. A 50 mm. 22G Neurography® needle (Radionics) is introduced in a lateral approach in the direction of the X-rays and advanced using the 'tunnel vision' technique (Figure 4). The direction of the C-arm is changed to AP and the canula is further introduced until the tip is projected just lateral from the imaginary extended line of the bony column of the zygapophyseal joints. After injection of 0.2-0.3 ml contrast medium (Iohexol, Omnipaque 240®) showing the outline of the C2 segmental nerve, 0.5 ml. Lidocaine 2% is slowly injected. Assessment of headache relief is 30 minutes after the procedure.



**Figure 4**

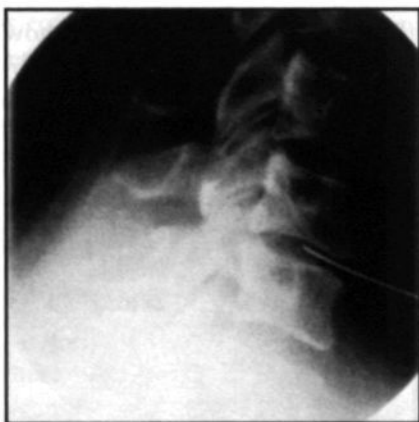
Diagnostic segmental nerve block C2. C-arm in lateral projection. The needle is projected as a dot in 'tunnel vision' technique.

### *Technique of a diagnostic disc block*

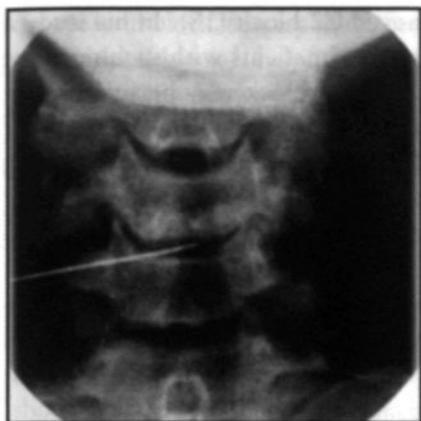
A diagnostic cervical disc block is performed with the patient in a supine position on the operating table. We use the analgesic discography technique to assess adequate headache relief. Using radiological control, the C-arm is positioned in a 50° oblique projection (24, 33). Projection of the disc without double contours is reached by changing the projection along the horizontal axis. At the selected disc level an entry point is marked, the carotid vessels are displaced laterally and a SMK-C5 (Sluijter-Metha Kit, Insulated Cannula 5 cm.) needle is introduced at the right side approaching from anterior. The needle passes the vessels medially and is carefully advanced under 'tunnel vision' fluoroscopy technique until the tip is close to the disc. After entering the disc the needle is advanced slightly farther until the tip lies in the middle of the disc on both the lateral and AP projections (Figure 5 and 6). When the needle is in correct position 0.5-1.0 ml. of a mixture of two parts of Lidocaine 2% and one part of Iohexol (Omnipaque 240®) is injected. During injection of this mixture continuous fluoroscopy is performed to prevent leakage from the disc to the epidural space. Assessment on headache relief is performed after 30 minutes. A diagnostic block of the cervical intervertebral disc is routinely performed from the right side to prevent perforation of the oesophagus, since the oesophagus is situated to the left of the median line (34). There is an increased risk of a discitis when a perforation of the oesophagus or pharynx occurs.

Figure 5

Diagnostic disc block C5-C6.  
Needle in the centre of the disc  
with C-arm in lateral projection.



The anterior approach is not suitable for the upper two levels, since it carries the risk of puncturing the pharynx (24). The approach of choice for the levels C2-C3 and C3-C4 is to introduce the needle from posterior to the carotid vessels in a slightly oblique projection. The procedure is continued as described above. The posterior-lateral approach of the higher disc levels has, on occasion, been found technically impossible due to a large uncinat process.



**Figure 6**

Diagnostic disc block C5-C6.  
Needle in the centre of the disc  
with C-arm in AP projection.

## DISCUSSION

Diagnostic blocks are included in the recently published criteria to diagnose CEH. At first sight diagnostic blocks seems to be the obvious method to confirm the diagnosis CEH. However, there are some practical problems which limits its usefulness. Practical problems may lead to false-positive and false-negative diagnostic blocks. Reliable evaluation of diagnostic blocks implies that, apart from considerations such as small volumes of local anaesthetic solution and contrast dye, to prevent overflow to adjacent structures, patient report of pain reduction must be unequivocal (22, 23, 35). Furthermore, lack of communication between the doctor and the patient, patient involvement in litigation procedures, psychological factors, coexisting social problems and placebo responses may be other sources of false-positive blocks (36, 37). A false-negative block may result after incorrect needle placement such as inadvertent injection to far away from the target structure or intravascular injection of the local anaesthetic solution.

A positive diagnostic block is an important criterion to establish the diagnosis CEH, but it may also be an indicator to employ therapeutic modalities such as radiofrequency lesions (RF-lesions) or other surgical procedures. In a recently published prospective uncontrolled study it was demonstrated that radiofrequency cervical zygapophyseal joint neurotomy for patients with CEH could be a beneficial treatment (38). Van Kleef et al. demonstrated in a prospective double blind randomised study that RF-lesions adjacent to the dorsal root ganglion gave a significant reduction of the pain in patients with cervicobrachial pain (39). A definite conclusion about the value of RF-lesions in the cervical area can only be drawn from randomised clinical trials in patients with CEH.

According to Bovim et al., a diagnostic block of the GON, which is the medial branch of the C2 dorsal ramus, is more convenient to perform

and has less side effects than a diagnostic C2 block (18). In his study a complete effect of GON block, in 4 of the 5 patients with such response to C2 block, suggests that the simpler GON block may be sufficient in many patients with CEH. Bovim et al. performed the diagnostic blocks of the cervical segmental nerves according the technique of Moore, using anatomic landmarks and elicitation of paresthesias, without fluoroscopy and contrast dye (40). Disadvantage of this 'blind' technique is that one is not assured of the correct position of the needle and overflow to adjacent nervous structures with 1.5 ml. of local anaesthetic solution is not imaginary. A positive relation between the GON and the diagnostic segmental block of C2 using the technique as described above has not been established yet.

Just like Bovim et al. we routinely perform diagnostic blocks of the segmental nerves C2 and C3 in order to confirm the diagnosis CEH (23). Only when both diagnostic nerve blocks are negative the segmental nerves C4 and C5 are tested too. To evaluate the effect of a diagnostic block it is important not only to assess the headache relief reported by the patients but also to assess sensory deficit in the particular dermatome that was blocked in order to correlate both responses (22). The results of Bovim et al. demonstrated that the diagnostic block of the segmental nerve C2 is the most informative procedure which is in line with our clinical experience.

In analgesic discography a local anaesthetic solution is injected into a putatively symptomatic disc in an effort to relieve patient's (head)pain by anaesthetising its source (41). However, analgesic discography is still not considered as the golden standard to establish discogenic pain. Absolutely speaking, we do not exactly know what a positive analgesic discography means. Does it mean that the disc is actively the source of the headache? Is it possible that the pain arises from other structures in the same motion segment which is innervated by the same dorsal root ganglion and afferent nerve? Analgesic discography may be difficult to achieve because it relies on the diffusion of the local anaesthetic solution from the nucleus pulposus to the outer innervated portion of the annulus fibrosis (42). False-positive results can be obtained from uncontrolled leakage into the epidural space. Some authors consider analgesic discography useful in diagnosing the 'pathological' source (24, 43). Other authors abandon the analgesic discography as a diagnostic block (44). Patients who are prone to infectious complications of the intervertebral disc, e.g. chronic corticosteroid medication, diabetes mellitus etc., should be excluded for this procedure.

Although epidural anaesthesia is not considered as a diagnostic block in diagnosing CEH, epidural anaesthesia is used by some neurosurgeons to evaluate the degree of headache relieve for patients with severe hemicranial pain. They emphasise that only after a positive outcome of

the epidural block, surgery in the cervical region is justified. In their opinion this epidural block is helpful in diagnosing and localising the origin of the headache (20). However, with an epidural block it is difficult to block only one selected level at a time. To select the 'pathological' level a diagnostic segmental nerve block, using fluoroscopy and contrast dye, is a more reliable procedure. A segmental nerve block is more convenient for the patient as well as much more secure. Because life threatening situations can occur with a cervical epidural block, e.g. myelum puncture, epidural haematoma, intravascular injection etc., an intravenous canula, cardiovascular monitoring and equipment to intubate the patient should be available on site. In our opinion the diagnostic cervical epidural block should not be used in standard diagnostic work-up for CEH.

In summary, numerous nerve blocks may be used in the diagnostic work-up of CEH. Since exact data on sensitivity and specificity for most of these procedures do not exist it is recommended to use the less complex ones first before moving to the more invasive techniques. Careful assessment of each diagnostic nerve block is essential.

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## CHAPTER 7

### **Radiofrequency cervical zygapophyseal joint neurotomy for cervicogenic headache: a prospective study of 15 patients**

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## ABSTRACT

The present study assessed the clinical efficacy of radiofrequency cervical zygapophyseal joint neurotomy in patients with cervicogenic headache. Fifteen consecutive patients with cervicogenic headache were treated and then assessed one week prior to treatment and, at short term (8 weeks), intermediate (mean 8.8 months) and long term (mean 16.8 months) follow-ups. The following were taken as outcome parameters Visual Analogue Scale (VAS), 7-point Verbal Rating Scale (VRS), number of headache days per week and analgesic intake per week.

The results of this study showed that radiofrequency neurotomy of the cervical zygapophyseal joints significantly reduced headache severity in 12 (80%) patients, both at short term and long term follow-up assessed by 7-point VRS. Mean VAS decrease was 31.4 mm. ( $p < 0.001$ ) and 53.5 mm. ( $p < 0.0001$ ) respectively in this period. The average mean number of headache days per week decreased from 5.8 days to 2.8 days ( $p = 0.001$ ) and the average analgesic intake per week showed a reduction from a mean of 17.5 tablets to a mean of 3.4 tablets ( $p = 0.003$ ).

A definitive conclusion about the clinical efficacy of this treatment can only be drawn from a randomized controlled trial.

**Keywords:** Cervicogenic headache, radiofrequency lesions, treatment

## INTRODUCTION

Despite its long history, the concept of cervicogenic headache (CEH), i.e. headache originating from putative abnormalities in the cervical spine, is still highly controversial. The early publications of this hypothesis, that head pain could originate from structures in the neck, include works by Barré, Bärtschi-Rochaix and Hunter and Mayfield in the first half of the century (1-3). In this hypothesis, the crucial feature distinguishing CEH from the other headache syndromes is the concept that the pain originates from a structural abnormality in the cervical spine. Consequently, therapy has largely been surgical, attempting to correct putative abnormalities in the cervical spine. Numerous therapeutic procedures for CEH have been published, including neurolysis of the major occipital nerve, cervical rhizotomy, decompression of C2 root and ganglion and cervical zygapophyseal joint denervation (4-7).

Since many of these studies were not controlled and did not include precise description of diagnostic criteria, this vast body of literature only added to the controversy surrounding CEH.

Criteria for the diagnosis of CEH were published by Sjaastad et al. in 1990, thus enabling researchers to select patients rigorously for future trials (8, 9). These diagnostic criteria are entirely clinical as the pathogenesis of CEH remains unknown. Various structures in the cervical spine, such as the zygapophyseal joints, intervertebral discs, root ganglia, muscles and ligaments are capable of causing neck pain and headache (10-14). Of all possible cervical structures, the zygapophyseal joints are probably the most accessible targets for invasive therapy. In particular, cervical zygapophyseal joint neurotomy by radiofrequency is a procedure which is generally easy to control and which has no clinically recognisable side effects, furthermore it has recently been shown to be effective in treating another cervical pain syndrome, namely post-whiplash syndrome (15).

The aim of this prospective open study was to assess the clinical efficacy of radiofrequency cervical zygapophyseal joint neurotomy in patients with CEH, diagnosed according to the current criteria (9).

## PATIENTS AND METHODS

### *Patients*

Fifteen consecutive patients (4 males and 11 females) with CEH were studied in the period from January 1996 to July 1996. Patients were seen at the outpatient clinic of the Pain Management and Research Centre of the University Hospital of Maastricht, The Netherlands. Patients were referred by neurologists and general practitioners. All patients were diagnosed by a neurologist (W.W) according the diagnostic criteria, set out by Sjaastad et al. in 1990. Details of the sample are given in Table 1. All patients

had undergone conservative treatment without any appreciable positive result i.e. without relief of their headache. Conservative treatment consisted of analgesic medication, physical and/or manipulative therapy and sometimes TENS (Transcutaneous Electrical Nerve Stimulation).

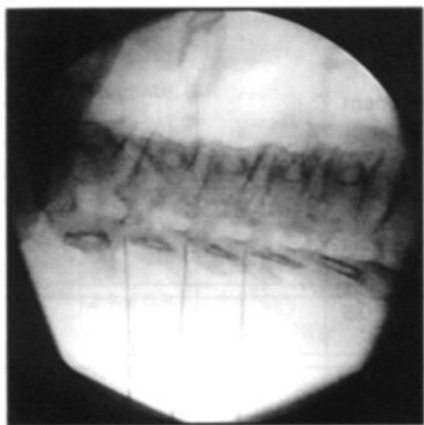
Table 1. Details of the sample.

Number of patients	15	Cervicogenic headache	
Females/males	11/4	unilateral	12
Age range	23 - 75	bilateral	3
(mean)	(56.0 years)		
Duration of headache		Head/neck trauma	
6-36 months	5	yes	3
36-60 months	1	no	12
> 60 months	9		

### *Technique*

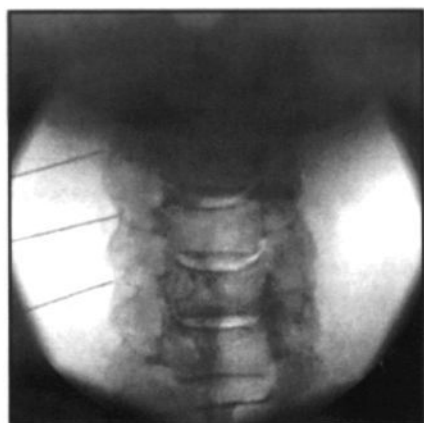
Therapy consisted of a radiofrequency (RF) lesion of the medial branch of the dorsal ramus of the segmental nerve at the levels C3 to C6 on the symptomatic side. For RF-lesions of the cervical dorsal ramus, the patient is positioned supine on the operating table. To reach the medial branch of the dorsal ramus, a C-arm intensifier (Type Philips BV-25, Eindhoven, The Netherlands) is used in an oblique position, as proposed by Sluijter (16, 17). The dorsal ramus runs over the base of the superior articular process. The entry point of the electrode is marked approximately 1 cm. posterior to the posterior border of the facet column and slightly caudal to the target point. Under fluoroscopic guidance, the electrodes (TOP XE 6 needles, active tip 5 mm.) are carefully introduced and advanced anteriorly and cranially until contact is made with the facet column at the target point (Figure 1). The position of the C-arm is changed to the anterior-posterior (AP) direction. This should confirm the position of the tip of the electrode adjacent to the waist of the ipsilateral articular pillars of the spine at the corresponding level (Figure 2). After this anatomical localization a physiological control with electrostimulation is carried out. Sensory stimulation at a rate of 50 Hz should elicit a response in the neck at < 0.7 Volt. When this criterium was not met we repositioned the electrode until sensory stimulation elicited a response in the neck at < 0.7 Volt.

On motor stimulation at 2 Hz, there must be no muscle movement in the ipsilateral shoulder/arm. If these criteria are met, the medial branch of the dorsal ramus is anesthetised with 1-2 ml. local anesthetic solution (Lidocaine 1%), and a 20 Volt RF-lesion is made for 60 seconds at each level (Radionics RFG-3C, Burlington, MA).



**Figure 1.**

Cervical zygapophyseal joint denervation: C-arm in 20°-30° oblique and 10° caudocranial projection. Electrodes make contact with bone at the base of the superior articular processes.



**Figure 2.**

Cervical zygapophyseal joint denervation: C-arm in anterior-posterior projection. Electrodes adjacent to the waist of the articular pillars of the cervical spine.

### *Outcome parameters*

Pain intensity was measured by Visual Analogue Scale (VAS) and 7-point Verbal Rating Scale (VRS) (Table 2), before treatment, 8 weeks after treatment, 4 to 14 months after treatment (mean  $8.8 \pm 2.83$ ) and 12 to 22 months after treatment (mean  $16.8 \pm 2.83$ ). Other outcome parameters, assessed at the same intervals, were:

1. the mean number of days with headache per week (i.e. the week immediately prior to the follow-up).
2. the mean analgesic intake per week (i.e. the last week immediately prior to the follow-up).

Analysis was performed with the statistical software package for social sciences (SPSS 7.0). P-values are reported one tailed. Treatment effects were tested with paired T-tests.



Table 2. Results of treatment.

	pre-treatment No = 15	short-term (8 weeks) No = 15
<b>Visual Analogue Scale</b> (mean VAS scores in mm.)	90.4 $\pm$ 2.3	59.0 $\pm$ 7.8
<b>Headache days</b> (mean days per week)	5.8 $\pm$ 0.5	3.7 $\pm$ 0.7
<b>Analgesic consumption</b> (mean tablets per week)	17.5 $\pm$ 3.9	10.5 $\pm$ 3.6
<b>Verbal Rating Scale</b>		
- complete relief		1
- good relief		11
- little relief		0
- no relief		3
- little worse		0
- much worse		0
- excruciating		0

Values are mean  $\pm$  SEM

## RESULTS

Short term follow-up 8 weeks after treatment revealed complete (no=1) and good pain relief (no=11) in 12 (80%) patients and no pain relief in 3 (20%) patients, assessed by 7-point VRS. At the 8-week follow-up, mean VAS decrease (meaning pain relief) was 31.4 mm. ( $p < 0.001$ ) (Table 2). Follow-up at 4 to 14 months showed complete (no=4) and good (no=8) pain relief in 12 patients and no pain relief in 3 patients (these 3 patients also reported no pain relief at the 8 week interval). Mean VAS decrease at this follow-up was further improved to 54.3 mm. ( $p < 0.0001$ ). Long-term follow-up at 12-22 months revealed complete (no=1) or good pain relief (no=8) in 9 (60%) patients, little relief in 2 subjects and no pain relief in 3 patients. Mean VAS decrease at long-term follow-up was 53.5 mm. ( $p < 0.0001$ ). One patient who had sustained a motor vehicle accident with severe neck pain was lost to follow-up 18 months after treatment.

The average mean number of headache days per week (last week prior to treatment) per person was 5.8 days (range 1-7) before treatment. At the 8 week follow-up this number had decreased to 3.7 days (range

intermediate (4 - 14 months) No = 15	long-term (12 - 22 months) No = 14
36.1 ± 8.8	36.9 ± 7.3
2.1 ± 0.8	2.8 ± 0.8
7.4 ± 3.5	3.4 ± 1.4
4	1
8	8
0	2
3	3
0	0
0	0
0	0

0-7,  $p=0.0015$ ). A further decrease, to 2.1 days (range 0-7), was observed at 4-14 months. This decrease in the number of headache days was statistically significant ( $p< 0.0001$ ). The last follow-up at 12-22 months showed a slight increase to 2.8 days (range 0-7,  $p=0.001$ )

The mean analgesic intake per week (the week immediately prior to treatment) per person was 17.5 tablets (range 1-45) before treatment. This was reduced, 8 weeks after treatment to 10.5 tablets (range 0-45,  $p=0.0025$ ) and to 7.4 tablets (range 0-45) at follow-up after 4-14 months. This mean reduction in analgesic consumption for headache relief was statistically significant ( $p=0.001$ ). At the final follow-up at 12-22 months the mean analgesic intake was 3.4 tablets (range 0-19,  $p=0.003$ ), which still represented a significant reduction. Analgesics used, at least 6 months prior to treatment, by the patients were acetaminophen (no=5), Non Steroidal Anti Inflammatory Drugs (NSAID's) (no=9) and tramadol (n=1). Besides the NSAID's one patient used ergotamine and one patient used sumatriptan. Withdrawal of analgesics was not applied in this patient group before RF treatment.

Therapy failed in 3 female patients. One of those patients had a bilateral CEH and 2 patients had a unilateral CEH. None of these three patients had a history of head or neck trauma. All three patients had a high analgesic consumption ranging from 56 to 120 tablets per 4 weeks and in retrospect one of them fulfilled the criteria for drug abuse headache. Apart from their higher age (75, 72 and 68 years against the mean age of 56.0) characteristics of these patients were not markedly different from the responders.

Side effects were assessed. One patient reported a burning pain in the neck after the RF-lesion, which disappeared spontaneously after 1 to 2 weeks. Sensory/motor deficits did not occur in any patient.

## DISCUSSION

Although most researchers agree that headache may originate from abnormalities in the cervical spine, the concept of CEH is still controversial. This controversy was fueled both by lack of consensus about the diagnostic classification of CEH and lack of controlled studies. The diagnostic criteria published by Sjaastad et al. in 1990 enable researchers to select patients for future trials. We used these criteria to select patients with CEH for treatment with RF cervical zygapophyseal joint neurotomy. Since RF neurotomy of the cervical zygapophyseal joints appears a simple and safe technique this is the procedure of first choice to study in a randomized controlled trial (RCT). Moreover, the cervical zygapophyseal joints have been implicated in the pathogenesis of CEH, and denervation of these joints has recently been shown to be effective in another cervical pain syndrome (15).

We have now done a prospective open study to investigate the feasibility of such a RCT. We show here, in patients diagnosed according to the criteria, that RF neurotomy of the cervical zygapophyseal joints reduces headache both on a short- and long-term basis. These results are confirmed by a reduction of analgesic intake and of the average number of headache days/week. This positive effect appears to be maximal in the 4-14 months (mean 8.8) after treatment, with a tendency of some variables to worsen gradually in the long term. This observation is in accordance with data from a recently published RCT (15). Our median long-term follow-up was 16.8 months and there was one patient reporting recurrence of headache complaints who needed a second RF neurotomy of the cervical zygapophyseal joints on the same side after 17 months. A longer follow-up period is needed to assess the value of RF treatment in patients with CH. However, our study demonstrated that this RF neurotomy did not produce any serious side effects.

Our technique for producing the actual RF lesion differs from the one recently described by Lord et al. (18). These authors described a technique in which the electrodes were introduced parasagittally and at a

30-degree angle to the sagittal plane so that the electrodes were placed tangentially beside the articular pillar and more parallel to the target nerve with the patient in a prone position. Using this technique, the higher cervical area (C2-C3) is difficult to treat due to technical problems and each operation lasts about three hours. We use a posterolateral approach by oblique projection to reach the medial branch of the dorsal ramus (13, 19, 20). Advantages of this technique are: 1) the possible application of RF neurotomy at the C2-C3 zygapophyseal joint; 2) easy access to the origin of the medial branch with the patient in a supine position; 3) a proper distance between the electrode tip and the ventral ramus is safeguarded by using oblique projection visualising the intervertebral foramina; 4) the time for the procedure is 20-30 minutes. We always employ electrostimulation to verify electrode position. In a cadaver study, Stolker pointed out that the electrodes were found to be positioned in the vicinity of the target nerve in only 60% of the cases (21). He concluded that electrostimulation should always follow anatomical electrode positioning.

Another essential difference between the study by Lord et al. and our study is the use of diagnostic nerve blocks. We have not used diagnostic nerve blocks for the following reasons.

Firstly we employed strict clinical criteria to reach the diagnosis of CEH (9). Secondly diagnostic zygapophyseal branch blocks have been reported to be false positive in 27% of cases (22). In addition to Bogduk, Lord et al. advocate the use of double-blind, placebo-controlled blocks to reach a precise diagnosis of zygapophyseal joint pain (15, 23). However, the specificity of these diagnostic nerve blocks, used by Lord and co-workers, has not been validated in long-term studies of ablative procedures (24). North et al. confirmed that false positive results are common with nerve blocks used to localise or diagnose sources of pain and that the sensitivity and specificity of such blocks are low (25). This is especially true for diagnostic cervical zygapophyseal nerve blocks (21).

This prospective open study demonstrates that RF cervical zygapophyseal joint neurotomy leads to a significant reduction in headache severity, in the number of days with headache and in analgesic intake in patients with CEH diagnosed according to the criteria of Sjaastad et al. (9). A substantial proportion of our patients consumed high amounts of analgesics. As is the case with most types of headaches, probably also CEH can lead to analgesics abuse, thus transforming the headache into a chronic daily (drug induced) headache. In our prospective RCT we will exclude patients with possible drug induced headache. However, a definitive conclusion about the clinical efficacy of the procedure can only be drawn from a randomized controlled trial, which is currently underway.

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## CHAPTER 8

### General discussion



Cervicogenic headache (CEH) is a clinically defined headache syndrome that is hypothesised to originate from nociceptive structures in the cervical or occipital area. Despite its long history, and many clinical studies and reports, the concept of CEH is still controversial. This controversy is reflected in the acceptance of CEH as a separate headache syndrome by the two major organisations concerned with head pain. The International Association for the Study of Pain (IASP) classification does include CEH as a primary headache syndrome. In contrast, the International Headache Society (IHS) classification considers the concept of CEH, according the criteria from Sjaastad et al., as not sufficiently validated in the absence of demonstrable neck pathology. Instead the IHS classification only includes 'headache associated with disorder of the neck', in order to accommodate headaches in close relation to a disorder in the neck. In 1998 Sjaastad and co-workers formulated stringent clinical criteria for the diagnosis of CEH.

In 1997 we decided to investigate several aspects related to the concept of CEH with the aim to achieve more substantiated evidence supporting this headache concept. Research questions were:

- Can CEH be diagnosed in a reliable way when one uses the Sjaastad criteria?
- Can physical examination of the cervical spine, a substantial part of the diagnosis CEH, be assessed reliably?
- What is the 'disease burden', i.e. impact on quality of life, of CEH?
- Which diagnostic nerve block has to be performed in CEH?
- Is cervical zygapophyseal joint neurotomy a potential effective therapy for CEH?

## RELIABLE ASSESSMENT OF CEH DIAGNOSIS

The IHS classification has been shown to provide satisfactory interobserver reliability for the diagnosis of primary headaches. However, reliability for CEH diagnosis according to the criteria of Sjaastad et al. had never been assessed. We employed an 'in vivo' study to assess diagnostic validity of the CEH concept. In this 'in vivo' study, examining 'live' headache patients like in routine daily clinical practice, we found that the reliability in diagnosing CEH, when strictly applying the criteria from Sjaastad et al., is similar to the reliability in diagnosing migraine without aura and tension-type headache according the IHS criteria. In this study physicians had most difficulty to diagnostically delineate patients with tension-type headache from CEH and migraine sufferers. This implies that using the criterion 'unilaterality without sideshift' in the diagnostic work-up of headache facilitates the recognition of CEH. This criterion is therefore an absolute requirement for the diagnosis of CEH for research purposes.

## RELIABLE ASSESSMENT FOR PHYSICAL EXAMINATION OF THE CERVICAL SPINE

Physical examination of the cervical spine is a substantial part of the diagnostic process in CEH. Therefore it is important to assess whether cervical spine examination in headache patients can be performed in a reliable manner in the absence of a 'reference standard'. Because physical examination tests of the cervical spine are not relevant for the majority of headache diagnoses, most headache neurologists are not experts in this field. Hence, the question arises whether the criteria from Sjaastad and co-workers, regarding specific items pertaining to cervical spine examination, can be applied reliably by expert headache neurologists without specific training. It is shown in our study that the interobserver reliability of the headache neurologists in the majority of cervical spine examination tests in headache patients is sufficient. To increase reliability and to make results between studies more comparable standardisation of the clinical tests is recommended. A standardised clinical examination of the cervical spine and occipital area may reveal the origin of the headache and can serve as an indicator of which diagnostic anaesthetic blocks need to be performed.

## QUALITY OF LIFE IN CEH PATIENTS

CEH is defined as a clinical headache syndrome that is hypothesised to originate from nociceptive structures in the cervical or occipital area. But what does it really mean to the patient to have CEH? An instrument to assess this is 'health-related quality of life' (HRQoL). Recently, the clinical relevance and feasibility of collecting such information from headache patients has received considerable attention. Methods to collect such data have advanced in previous years. The SF-36 questionnaire is the most widely used generic instrument to assess HRQoL for headache syndromes. Our data demonstrate that the impairment in HRQoL is worse in CEH patients compared with healthy individuals, but is, in general, comparable with migraine and tension-type headache. Our study suggests that the SF-36 is a reliable and valid measure of HRQoL in patients with CEH, and it may prove to be valuable in studying the efficacy of therapy in patients with CEH.

## TECHNIQUES OF DIAGNOSTIC NERVE BLOCKS IN CEH

Recently, refinements of the diagnostic criteria for CEH by Sjaastad and co-workers were published, emphasising the use of diagnostic nerve blocks as important confirmatory evidence in diagnosing CEH. These diagnostic blocks should relate to nerves and/or structures suspected of medi-

ating of causing headache. A positive diagnostic block is an important criterion to establish the diagnosis CEH. It may also be an indicator for therapeutic modalities such as RF-lesions or other surgical procedures, and for the appropriate localisation of the procedure. At present controversy remains whether these blocks must be administered as single anaesthetic blocks or as comparative local anaesthetic blocks or in a double-blinded placebo-controlled manner. This last mode of action is not patient-friendly and leads to a considerable increase of costs, as the patient has to be treated in multiple sessions.

## AN EFFECTIVE TREATMENT FOR CEH

Because CEH is hypothesised to emanate from nociceptive structures in the cervical spine, therapy has largely been surgical, especially for patients in whom conservative treatment has failed. To establish a specific, curative therapy for CEH, increased knowledge on the aetiology and pathophysiology of CEH is needed. However, as long as this knowledge is not available, therapy should aim to be as effective as possible without serious side effects. The approach of the different invasive (surgical) therapies can be divided in:

- Surgical 'decompression' techniques of nerves and ganglia
- Local injection therapy with local anaesthetics around nerves
- Radiofrequency (RF) lesions of nerve structures

The surgical 'decompression' procedures are considered to be more or less 'causal' related therapies, while the RF-lesions and 'local injections' can be considered as symptomatic treatment modalities. However, RF-lesions as well as 'local injections' are much less invasive compared to the surgical (vascular) 'decompression' procedures. Disadvantage of the 'local injections' is the temporary effect of this therapy varying from one to seven days, while the duration of efficacy of RF-lesions tends towards minimally one year with some decline afterwards. To compare different therapies, it is important that the diagnosis CEH is reached by using the same criteria i.e. from Sjaastad and co-workers in order to have homogeneous groups. The reliability of these criteria for diagnosing CEH has been proven elsewhere in this thesis.

At present, for lack of randomised controlled trials of the therapeutic surgical techniques no statement can be made as to their effectiveness. Therefore reasoning pragmatically and considering patient comfort, one could argue to use a less invasive procedure, such as RF-lesions, as a first treatment option before a more invasive 'decompression' operation.

## FUTURE RESEARCH

Some questions have been answered, and many others have been raised by our studies. Future fields of research will include:

- Epidemiological studies in general populations are required to assess the true prevalence and incidence of CEH
- A pathophysiological model to clarify the relation between headache and the cervical spine needs to be developed.
- Standardisation of clinical tests for physical examination of the cervical spine in headache patients.
- The value of single diagnostic anaesthetic nerve blocks compared with double blinded placebo-controlled blocks in headache patients.
- The relation between the accuracy of physical examination in order to predict the involved symptomatic structure and specification of the level.
- Efficacy of different treatments should only be measured by randomised controlled trials.

## FINAL CONCLUSION

In contrast with previous belief that CEH is not a separate headache syndrome, we have shown that CEH can reliably be delineated diagnostically from migraine and tension-type headache if the criteria from Sjaastad et al. are correctly applied. Furthermore, the present data demonstrate that physical examination of the cervical spine and occiput can reliably assessed. These findings i.e. anamnestic and physical signs, show that the diagnostic concept, is validated.

We have summarised the literature on techniques for the diagnostic anaesthetic nerve blocks and have made suggestions for standardisation of these blocks in the diagnostic work-up of CEH. In our prospective study we have shown that RF neurotomy of the medial branch of the dorsal ramus at the zygapophyseal joint may be an efficacious therapy in CEH. Recently, a prospective randomised controlled trial (RCT) regarding RF neurotomy, at the medial branches of the dorsal rami at the zygapophyseal joints on the symptomatic side in patients with CEH, has been started in our pain clinic. The 'burden of disease' for CEH is substantial compared with healthy individuals. Compared with migraine and tension-type headache quality of life reduction is the same.

Further research regarding the aetiology and pathophysiology as well as an efficacious treatment are required to establish the concept of CEH.



## CHAPTER 9

### Summary

The studies presented in this thesis aimed at scientifically validating the concept of cervicogenic headache (CEH) as a distinct headache syndrome.

## CHAPTER 1. INTRODUCTION

The introduction starts with a description of Hippocrates' concepts about headache in the ancient Greek world. Although our view about headache has changed since then, the precise pathophysiological substrate for the different headache syndromes still needs to be established. Sjaastad et al. introduced the term CEH in 1983. However, despite a bulk of literature regarding CEH, the concept of CEH remains controversial. The chapter concludes with defining the aims of this thesis in order to investigate and clarify some controversies around CEH.

## CHAPTER 2. CERVICOGENIC HEADACHE: A REVIEW

This chapter gives a critical review of the literature on CEH. It presents a historical overview of research on headaches originating from the neck, from the second half of the nineteenth century up to the present time. It describes the nomenclature, epidemiological data, the clinical symptoms and diagnostic criteria for CEH. An overview regarding potential pathophysiology i.e. mechanisms in CEH is given. Next, items for the traditionally performed patient history and physical examination are presented. The value of different X-ray investigations and neurophysiological techniques is summarised. The differential diagnosis for CEH is discussed. Finally a detailed review of the therapeutic state of the art for CEH in 2000 is given.

## CHAPTER 3. INTEROBSERVER RELIABILITY OF DIAGNOSTIC CRITERIA FOR CERVICOGENIC HEADACHE

To assess the interobserver reliability in distinguishing CEH from migraine without aura and tension-type headache we conducted an 'in vivo' study. The 'in vivo' study design, examining 24 'live' headache patients by 6 physicians, resembles routine daily clinical practice as close as possible. During a session, each physician performed a physical examination and queried six patients in succession using a semi-structured interview. Diagnosis of the headache disorders was carried out in accordance with the International Headache Society (IHS) criteria for migraine without aura and tension-type headache and the criteria from Sjaastad et al. for CEH. Kappa statistics for agreement on diagnosis were used: 0.83 between the expert headache neurologists; 0.74/0.73 between the expert anaesthesiologist in (head) pain treatment and both expert neurologists

respectively; kappa ranged from 0.43 to 0.62 between the other physicians. The results of our 'in vivo' design study show that the reliability in diagnosing CEH, when strictly applying the criteria from Sjaastad and co-workers, is similar to the reliability in diagnosing migraine and tension-type headache according the IHS criteria.

#### CHAPTER 4. INTEROBSERVER RELIABILITY IN PHYSICAL EXAMINATION OF THE CERVICAL SPINE IN PATIENTS WITH HEADACHE

The diagnosis CEH involves a physical examination of the cervical spine. In the absence of a 'reference standard' for physical examination of the cervical spine it is imperative that acceptable levels of agreement must be obtained to establish its diagnostic relevance. Therefore, we performed a study to assess the interobserver reliability between two expert headache neurologists when examining the cervical spine of patients with headache. Twenty-four patients diagnosed as having CEH, migraine without aura and tension-type headache were included. After a semi-structured interview, each patient's cervical spine was examined in a structured way. Reliability was assessed by Cohen's kappa. Our study showed that the interobserver reliability of both expert headache neurologists was satisfactory in the majority of the physical examination tests of the cervical spine in patients with different headache disorders. However, we recommend further standardisation of the clinical tests to improve their reliability.

#### CHAPTER 5. QUALITY OF LIFE IN CERVICOGENIC HEADACHE - A COMPARISON WITH HEALTH SUBJECTS, MIGRAINE AND TENSION-TYPE HEADACHE PATIENTS

The purpose of this study was to establish the health-related quality of life (HRQoL) in patients with cervicogenic headache (CEH) and to compare it with a random Dutch sample of healthy persons (reference group), and with patients with migraine without aura or episodic tension-type headache. HRQoL is an expression of individuals' perceptions of their position in life that is affected by their physical health, psychological state and social relationships. We included 37 CEH patients, 42 episodic tension-type headache patients and 39 patients with migraine without aura. All patients completed the SF-36 questionnaire. Data from the healthy reference group were derived from a random sample survey from the population register of Emmen, a Dutch city in The Netherlands. We found that patients with CEH have a quality of life impairment that is substantial compared to healthy subjects. This impairment is comparable with migraine without aura and episodic tension-type headache. Our data suggest that the SF-36 questionnaire is valuable in determining differences



in quality of life among headache disorders and might be used as a primary outcome measure in clinical trials for CEH.

## CHAPTER 6. CERVICOGENIC HEADACHE: TECHNIQUE OF DIAGNOSTIC NERVE BLOCKS

Diagnostic nerve blocks are a cardinal feature in establishing the diagnosis of CEH since the revised criteria published in 1998. Therefore, standardisation of nerve blocks in the diagnostic work-up of CEH patients is essential. Besides that, a positive diagnostic block may also be an indicator for the etiological structure. A diagnostic block is a temporary (reversible) block with a local anaesthetic solution directed to nerves and/or structures suspected of mediating or causing the headache. In this paper we discuss problems such as false-positive and false-negative blocks which limit its usefulness. Although exact data on the sensitivity and specificity of most of these procedures do not exist, we present an overview of the local anaesthetic blocks in the cervical area in the diagnostic work-up of patients with CEH. Furthermore, it is recommended to start with less complicated blocks first before moving to the more invasive techniques.

## CHAPTER 7. RADIOFREQUENCY CERVICAL ZYGAPOPHYSEAL JOINT NEUROTOMY FOR CERVICOGENIC HEADACHE: A PROSPECTIVE STUDY IN 15 PATIENTS

This prospective study reports the clinical efficacy of radiofrequency (RF) cervical zygapophyseal joint neurotomy in patients with CEH. Of all possible cervical structures, the zygapophyseal joints are probably the most accessible targets for invasive RF therapy. All 15 patients were diagnosed by a neurologist and had undergone conservative treatment without positive result. The results of this study showed that RF neurotomy of the cervical zygapophyseal joints significantly reduced the headache in 12 (80%) at short-term follow-up (8 weeks) and intermediate-term follow-up (mean 8.8 months) and 9 (60%) patients at long-term follow-up (mean 16.8 months) assessed by 7-point Verbal Rating Scale. Mean Visual Analogue Scale (VAS) decreases were 31.4 mm ( $p < 0.001$ ), 54.3 mm ( $p < 0.001$ ) and 53.5 mm ( $p < 0.0001$ ) respectively in these periods. The other parameters such as headache days per week and analgesic consumption per week showed all a significant reduction during long-term follow-up. However, this study shows that there a tendency of some variables to worsen gradually in the long-term follow-up period. A definitive conclusion about the clinical efficacy of this treatment can only be drawn from a randomised controlled trial, which is currently underway in our centre.

## CHAPTER 8.GENERAL DISCUSSION

In this chapter the overall findings of this thesis are briefly discussed. Development of standards is recommended for: 1) physical examination of the cervical spine; 2) the technique of diagnostic nerve blocks with a local anaesthetic solution. Our data show that the diagnostic concept of CEH, using the criteria from Sjaastad et al., is validated.

In this chapter the overall features of the three new models are discussed. The first model is a simple extension of the two-body model. The second model is a more sophisticated extension of the two-body model. The third model is a more sophisticated extension of the two-body model. The first model is a simple extension of the two-body model. The second model is a more sophisticated extension of the two-body model. The third model is a more sophisticated extension of the two-body model.

## CHAPTER 10

### **Samenvatting**

In dit proefschrift worden de resultaten beschreven van de verschillende studies met als doel om het concept van cervicogene hoofdpijn (CEH), zijnde een (unilateraal) primair hoofdpijn syndroom, nader te onderbouwen op een wetenschappelijke manier.

## HOOFDSTUK 1. INTRODUCTIE

De introductie begint met een historische beschrijving betreffende de ideeën van Hippocrates over hoofdpijn in de Griekse oudheid. Ofschoon onze hedendaagse visie over hoofdpijn geheel verschillend is met die van Hippocrates, is het exacte pathofysiologische substraat voor de verschillende hoofdpijn syndromen nog steeds niet geheel opgehelderd. In 1983 werd door Sjaastad et al. het concept van cervicogene hoofdpijn (CEH) geïntroduceerd. Echter, ondanks een grote hoeveelheid literatuur omtrent CEH, is het concept van CEH nog controversieel. Vervolgens worden in hoofdstuk 1 de doelstellingen van dit proefschrift geformuleerd.

## HOOFDSTUK 2. CERVICOGENE HOOFDPIJN: EEN OVERZICHT

Dit hoofdstuk geeft een kritisch overzicht van de internationale literatuur over CEH. Allereerst wordt een historische overzicht gepresenteerd over het concept hoofdpijn komende vanuit de nek vanaf de tweede helft van de 19e eeuw tot heden. Vervolgens wordt een literatuuroverzicht gegeven van CEH betreffende: nomenclatuur, epidemiologie, klinische symptomen, diagnostische criteria, pathofysiologie, anamnese, lichamelijk onderzoek, diagnostisch röntgen onderzoek, neurofysiologisch onderzoek en differentiële diagnostiek. Tot slot wordt een 'state of the art' overzicht gegeven van de therapeutische mogelijkheden en resultaten voor CEH anno 2000.

## HOOFDSTUK 3. INTEROBSERVER BETROUWBAARHEID VAN DE DIAGNOSTISCHE CRITERIA VOOR CEH

Een 'in vivo' studie werd uitgevoerd om de interobserver betrouwbaarheid te beoordelen voor het vaststellen van de diagnose CEH bij patiënten met migraine zonder aura, spanningshoofdpijn of CEH. De opzet van de 'in vivo' studie was om 24 hoofdpijn patiënten, gedurende 4 sessies, te laten onderzoeken door 6 artsen en wel op een manier die de dagelijkse klinische praktijk benadert. Tijdens een sessie nam iedere arts bij 6 patiënten achtereenvolgens een anamnese af met behulp van een semi-gestructureerde vragenlijst en voerde hierna een lichamelijk onderzoek van het hoofd en de nek uit. De diagnose werd gesteld overeenkomstig de hiervoor geldende criteria van de International Headache Society (IHS) voor migraine zonder aura en spanningshoofdpijn en de criteria van

Sjaastad et al. voor CEH. Als maat voor de interobserver betrouwbaarheid werd gebruik gemaakt van 'kappa'. Kappa is een statistische variabele die ontwikkeld is door Cohen om overeenstemming tussen waarnemers te meten, rekening houdend met de mate van toevallige overeenstemming. De kappa-waarden in deze studie waren: 0,83 tussen de 'expert' hoofdpijn neurologen; 0,74/0,73 tussen de 'expert' anesthesioloog voor (hoofd)pijn en de beide 'expert' neurologen respectievelijk; tussen de andere medisch specialisten varieerden de kappa-waarden tussen 0,43 en 0,62. De resultaten van onze 'in vivo' studie tonen aan dat de betrouwbaarheid voor het diagnostiseren van CEH, indien de criteria van Sjaastad et al. juist worden toegepast, gelijk is aan de betrouwbaarheid voor het diagnostiseren van migraine en spanningshoofdpijn volgens de IHS criteria.

#### HOOFDSTUK 4. INTEROBSERVER BETROUWBAARHEID VAN HET LICHAAMELIJK ONDERZOEK VAN DE CERVICALE WERVELKOLOM BIJ PATIËNTEN MET HOOFDPIJN

Voor het stellen van de diagnose CEH is het verrichten van een lichamelijk onderzoek van de cervicale wervelkolom en de occipitale regio essentieel. Een standaard voor het lichamelijk onderzoek van de cervicale wervelkolom is er momenteel nog niet. Gezien de diagnostische relevantie hiervan bij CEH is het belangrijk dat de betrouwbaarheid van dit lichamelijk onderzoek acceptabel is. Daarom hebben we een studie uitgevoerd, met 2 'expert' hoofdpijn neurologen, om de interobserver betrouwbaarheid van het lichamelijk onderzoek van de cervicale wervelkolom te meten bij patiënten met hoofdpijn. In de studie zijn 24 patiënten geïnccludeerd met migraine, spanninghoofdpijn of CEH. Nadat een semi-gestructureerde anamnese was afgenomen, werd bij iedere patiënt een lichamelijk onderzoek van de cervicale wervelkolom en de occipitale regio verricht op een gestructureerde wijze. De betrouwbaarheid werd gemeten middels kappa. Onze studie toonde aan dat de interobserver betrouwbaarheid tussen de beide 'expert' hoofdpijn neurologen bevredigend was in de meerderheid van de testen bij het lichamelijk onderzoek van de cervicale wervelkolom en occipitale regio bij patiënten met verschillende soorten hoofdpijn. Echter, het is aan te bevelen om een verdergaande standaardisatie te ontwikkelen van deze klinische testen bij patiënten met hoofdpijn om hun betrouwbaarheid te vergroten.

## HOOFDSTUK 5. DE KWALITEIT VAN LEVEN BIJ CERVICOGENE HOOFDPIJN PATIËNTEN – EEN VERGELIJKING MET GEZONDE PERSONEN, MIGRAINE- EN SPANNINGSHOOFDPIJN PATIËNTEN

Het doel van deze studie was om de 'kwaliteit van leven' te meten bij patiënten met CEH en dit te vergelijken bij een groep gezonde Nederlandse personen (referentie groep) en bij patiënten met migraine zonder aura of episodische spanninghoofdpijn. De met de gezondheid samenhangende kwaliteit van leven is een begrip dat drie onderscheidbare aspecten omvat: fysieke, psychische en sociale gezondheid van de patiënt. In deze studie zijn geïncludeerd: 37 patiënten met CEH, 42 patiënten met episodische spanningshoofdpijn en 39 patiënten met migraine zonder aura. Er werd gebruik gemaakt van de gevalideerde Nederlandse SF-36 vragenlijst. Alle patiënten hebben de SF-36 vragenlijst volledig ingevuld. De scores van de gezonde referentie groep waren afkomstig van een aselekt getrokken steekproef uit het bevolkingsregister van de gemeente Emmen. Uit de studie bleek dat de 'kwaliteit van leven' van patiënten met CEH significant beperkt is voor alle domeinen vergeleken met de gezonde referentie groep. Deze beperkingen zijn globaal vergelijkbaar met die van patiënten met migraine zonder aura en patiënten met episodische spanningshoofdpijn, hoewel het domein 'fysiek functioneren' in onze studie significant verschillend was bij CEH t.o.v. migraine zonder aura en spanningshoofdpijn. Uit de studie blijkt tevens dat de SF-36 vragenlijst waardevol kan zijn bij het bepalen van de 'kwaliteit van leven' bij hoofdpijn patiënten en als zodanig gebruikt kan worden als een (primaire) uitkomstmaat voor klinisch onderzoek bij patiënten met CEH.

## HOOFDSTUK 6. CERVICOGENE HOOFDPIJN: DE TECHNIEK VAN DIAGNOSTISCHE ZENUW BLOKKADES

Sinds de publicatie van de gereviseerde criteria voor CEH in 1998 door Sjaastad et al. zijn diagnostische zenuw blokkades een belangrijk instrument om de diagnose CEH te bevestigen. Daarom is standaardisatie van diagnostische zenuw blokkades bij patiënten met CEH van essentieel belang. Bovendien kan een positief diagnostisch blok eventueel ook een indicatie geven over de hoofdpijn veroorzakende anatomische structuur. Een diagnostische zenuw blokkade is een tijdelijke zenuw blokkade waarbij een lokaal anestheticum wordt geïnjecteerd nabij een zenuw of anatomische structuur die een rol speelt bij de hoofdpijn. In dit artikel worden enkele problemen nader toegelicht die zich kunnen voordoen bij het verrichten van diagnostische zenuw blokkades en die de bruikbaarheid hiervan kunnen beperken. Begrippen als fout-positief en fout-negatief worden nader toegelicht. Hoewel exacte data omtrent de sensitiviteit en specificiteit van de meeste procedures niet bekend zijn,

presenteren we toch een overzicht van de diagnostische zenuw blokkades in de cervicale regio bij patiënten met CEH. De techniek van de diverse zenuw blokkades wordt uitgebreid besproken in dit artikel. Als richtlijn wordt aangegeven te starten met de meest eenvoudige diagnostische zenuw blokkades voordat men overgaat tot het verrichten van de meer invasieve blokkades.

## **HOOFDSTUK 7. CERVICALE FACET DENERVATIE MIDDELS RADIOFREQUENTE LESIES BIJ CERVICOGENE HOOFDPIJN: EEN PROSPECTIEVE STUDIE BIJ 15 PATIËNTEN**

Deze prospectieve studie beschrijft de effectiviteit van de cervicale facet blokkade middels radiofrequente (RF) lesies bij patiënten met CEH. Van alle mogelijke cervicale anatomische structuren zijn de cervicale facet gewrichten waarschijnlijk de meest toegankelijke 'targets' voor invasieve behandeling met RF lesies. De 15 patiënten met CEH werden allen gediagnosticeerd door een neuroloog. Alle patiënten waren conservatief behandeld zonder positief resultaat. De resultaten van deze studie tonen dat RF lesies van de cervicale facet gewrichten de hoofdpijn klachten beduidend doen verminderen bij 12 (80%) patiënten, gedurende de korte termijn follow-up (8 weken) en tussentijdse follow-up periode (gemiddeld 8,8 maanden), respectievelijk 9 patiënten (60%) gedurende de lange termijn follow-up periode (gemiddeld 16,8 maanden). Dit effect werd gemeten middels een 7-punts 'Verbal Rating Scale' (VRS). De gemiddelde daling op de 'Visual Analogue Scale' (VAS) bedroeg 31,4 mm. ( $p < 0,001$ ), 54,3 mm. ( $p < 0,001$ ) en 53,5 mm. ( $p < 0,001$ ) in de respectievelijke follow-up periodes. Andere parameters zoals het aantal hoofdpijn dagen per week en de analgetische consumptie toonden ook een significante reductie gedurende de tussentijdse follow-up en de lange termijn follow-up periode. Echter, gedurende deze studie werd een tendens zichtbaar dat sommige parameters, tijdens de lange termijn follow-up, langzaam verslechterden. Een gerandomiseerd gecontroleerde studie (RCT), betreffende cervicale facet blokkade middels RF lesies, bij patiënten met CEH zal een definitief antwoord moeten geven over de effectiviteit van deze behandeling.

## **HOOFDSTUK 8. ALGEMENE CONCLUSIE**

In dit hoofdstuk wordt ingegaan op de interpretatie van de resultaten van dit proefschrift. Ontwikkeling van een standaard bij CEH wordt voorgesteld voor: 1) het lichamelijk onderzoek van de cervicale wervelkolom en de occipitale regio; 2) de volgorde en techniek van diagnostische zenuw blokkades met een lokaal anestheticum. Dit proefschrift toont aan dat het diagnostisch concept van CEH, zoals voorgesteld door Sjaastad et al., beschouwd kan worden als een gevalideerd klinisch concept.





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## CURRICULUM VITAE

Johannes Antonie (Hans) van Suijlekom was born on 7 July 1959 in Raamsdonksveer, the Netherlands. He attended the secondary school at the Mgr. Frencken College in Oosterhout (Noord-Brabant) from 1971 to 1977. From 1977 to 1978 he studied Chemistry at the Technical University (TU) in Eindhoven whilst waiting to start his medical study. In 1978 he started his medical study at the Erasmus University in Rotterdam and obtained his medical degree in May 1985. He worked as an intern in surgery at the Merwede Hospital in Dordrecht (Head: Dr. J. de Gruyl) from May 1985 to March 1987. He started his training in anaesthesiology in April 1987 at the Wever Hospital in Heerlen (Head: F. Douze-Kohl) and from May 1991 he continued his training in the department of Anaesthesiology at the University Hospital Maastricht (Head: Prof. dr. S. de Lange). He was registered as an anaesthesiologist on October 1st 1991. From October 1991 to April 2001 he has been staff member in the department of Anaesthesiology at the University Hospital Maastricht. Since April 2001 he works as an anaesthesiologist in the Catharina Hospital in Eindhoven.



